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EDITORIAL

THE ORAL PATHOLOGIST—A SPECIALIST

During the past several years groups interested in a particular phase of dentistry have formed academies or societies to bring together practitioners with a common interest. In order to provide stature and establish recognition of their specific interests, these groups have petitioned the American Dental Association for the privilege of initiating specialty boards. The numerous requests to the A. D. A. for recognition of dental specialties create the serious problem of determining which groups truly represent a dental specialty and which groups are simply small facets of a larger area of dental practice—in other words, what constitutes a dental specialty and who should be recognized as specialists.

The problem is complex; what constitutes a specialty depends upon the perspective from which the problem is viewed and the objectives to be attained by establishing specialties. Another difficulty confronting those burdened with the problem is the determination of what constitutes the practice of each specific field. What constitutes the practice of oral pathology must be defined by the American Academy of Oral Pathology.

The practice of oral pathology can be divided into two phases—the didactic and the practical. Oral pathology is the study of oral disease, and it is basic to the practice of all phases of dentistry. It is upon our knowledge of oral disease that all diagnosis and treatment are predicated. If one does not have information relative to the basic processes of pathology and the special processes characteristic of specific diseases, he lacks criteria for the recognition and knowledge necessary for treatment. It is important in the training of dental students and practitioners to have a teacher of dentistry who is especially trained in basic and special pathology so that he may correlate pathologic principles with clinical practice. Such a teacher must have prolonged special training in both general and oral pathology in addition to knowledge of dental practice.

The practical phase of oral pathology is a diagnostic activity engaged in by one specially trained to prepare and interpret histologic materials for the recognition of various diseases. It also requires the carrying out and interpretation of other laboratory procedures used as aids to clinical and radiographic

examination. In some instances the oral pathologist may perform clinical examinations at the request of a practitioner to determine the nature of a disease process and to indicate what laboratory procedures should provide important diagnostic information. This practical service is rendered to all phases of dentistry and can be performed only by those especially trained in pathology and especially equipped to render such services. No other branch of dentistry is engaged in this activity, and no other practitioner is qualified to render such a service to dental patients. This fact should indicate that oral pathology is a dental specialty in which patients, practitioners, and students are provided with a service which can be rendered only by one specifically trained for this purpose.

The American Academy of Oral Pathology should be dedicated to the purpose of bringing together, for an exchange of recent information obtained through research and study, those interested in the field of oral pathology. Such information should also be made available to the general practitioner through publication of the proceedings in a journal designated for this purpose. The Academy should also sponsor meetings at which those specially trained in the field of oral pathology can exchange information and experience in the area of diagnostic and experimental pathology. The proceedings of such meetings should also be published in a specifically designated journal for the benefit of all who are engaged in the practice of pathology. The Academy should also stimulate interest in the study of pathology and the training of qualified teachers and practitioners of oral pathology.

It is through the publication of proceedings such as those recorded in this issue of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY that the Academy helps to fulfill its objectives and justifies its existence.

The American Academy of Oral Pathology.
Donald A. Kerr, Editor

PROCEEDINGS OF
THE AMERICAN ACADEMY OF ORAL PATHOLOGY

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UNUSUAL STOMADROMES—PACHYONYCHIA CONGENITA, LIPOID PROTEINOSIS, REITER'S SYNDROME, EPIDERMOLYSIS BULLOSA, BONNEVIE-ULLRICH-TURNER'S SYNDROME, AND MULTIPLE HEREDITARY TELANGIECTASIA

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WE HAVE used the word *stomadromes** to imply a syndrome, or symptom complex, that contains one or more oral components. The term is used in the same sense that "dermadrome" has been used by Wiener.[1]

A few of the more unusual stomadromes will be discussed and illustrated: (1) Pachyonychia congenita, (2) Lipoid proteinosis (Urbach-Wiethe's syndrome), (3) Reiter's syndrome, (4) Epidermolysis bullosa (Goldscheider's and Weber-Cockayne's syndromes), (5) Bonnevie-Ullrich-Turner's syndrome, and (6) Multiple hereditary telangiectasia (Osler-Rendú-Parkes Weber's syndrome).

PACHYONYCHIA CONGENITA†

Pachyonychia congenita is an unusual congenital and sometimes familial malady characterized by dystrophic changes in the fingernails and toenails; hyperkeratosis or callosities of the palms and soles, follicular keratosis of the acniform type, particularly about the knees and elbows; and hyperhidrosis, or excessive sweating, of the hands and feet. Occasionally, dystrophic changes are also observed in the hair or cornea. Verrucous lesions may appear on the elbows, but they are especially common on the lower extremities about the knees, popliteal fossae, lower legs, and ankles. Plantar bullae are not uncommon. (See Figs. 1 and 2.) According to the genetic studies of Jackson and Lawler,[3] a single dominant gene is the responsible factor.

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*Personal communication with Dr. L. Cahn indicates that he has been using the term for a number of years.

†An extremely brief review, as this syndrome was described in detail by us in a recent publication.[2]

The microscopic picture of the oral lesions is that of acanthosis, intracellular edema, parakeratosis, and absence of the stratum granulosum.

This is but one of several ectodermal dysplasias that manifest oral changes. There is a similar complex, known as the Cole-Rauschkolb-Toomey syndrome[4-7] or dyskeratosis congenita with pigmentation, dystrophia unguium, and

Fig. 1.

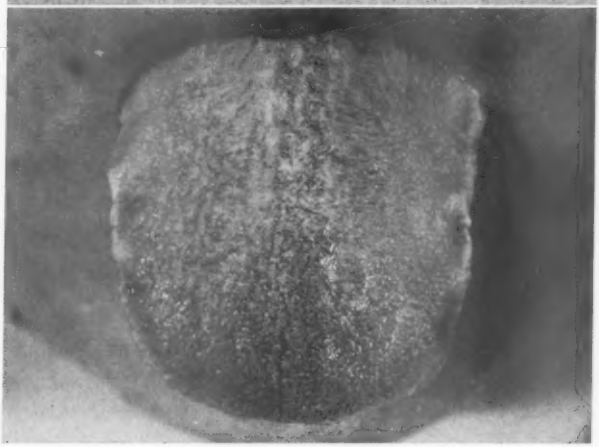


Fig. 2.

Fig. 1.—Pachyonychia congenita. Note thickened, darkly colored nails. This change was evident from birth. (From Gorlin and Chaudhry: ORAL SURG., ORAL MED. & ORAL PATH. 11: 541-544, 1958.)

Fig. 2.—Pachyonychia congenita. The patient's tongue was covered by a heavy white coat that did not rub off. The white epithelial thickening was especially apparent about the lateral margins. (From Gorlin and Chaudhry: ORAL SURG., ORAL MED. & ORAL PATH. 11: 541-544, 1958.)

leukokeratosis oris (Table I). From its salient features, similarities to other diseases will be noted. A recent article[7] links this condition with the hypersplenism of the Fanconi-Ehrlich syndrome.

TABLE I. COLE-RAUSCHKOLB-TOOMEY'S SYNDROME

1. Hyperhidrosis of palms and soles
2. Blisters and hyperkeratotic lesions of feet
3. Pigmentation of face, neck, forearms, and legs
4. Dystrophy of nails
5. Hyperkeratosis of oral mucosa
6. Lingual ulceration
7. Atrophy of tear ducts
8. Hypersplenism

LIPOID PROTEINOSIS (URBACH-WIETHE'S SYNDROME)

Lipoid proteinosis is an unusual disease of unknown etiology which has several oral features. Fewer than two dozen cases have been reported in the world literature.[8-16] Lipoid proteinosis is characterized initially in early infancy by the inability to cry. Later the voice assumes a hoarse whisper. The tongue is firm, wooden in consistency, and usually bound down to the floor of the

Fig. 3.

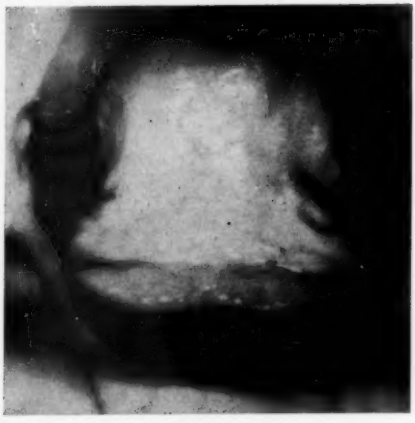


Fig. 4.

Fig. 3.—Lipoid proteinosis. Note numerous raised plaques on lips. These were yellowish in color and firm.

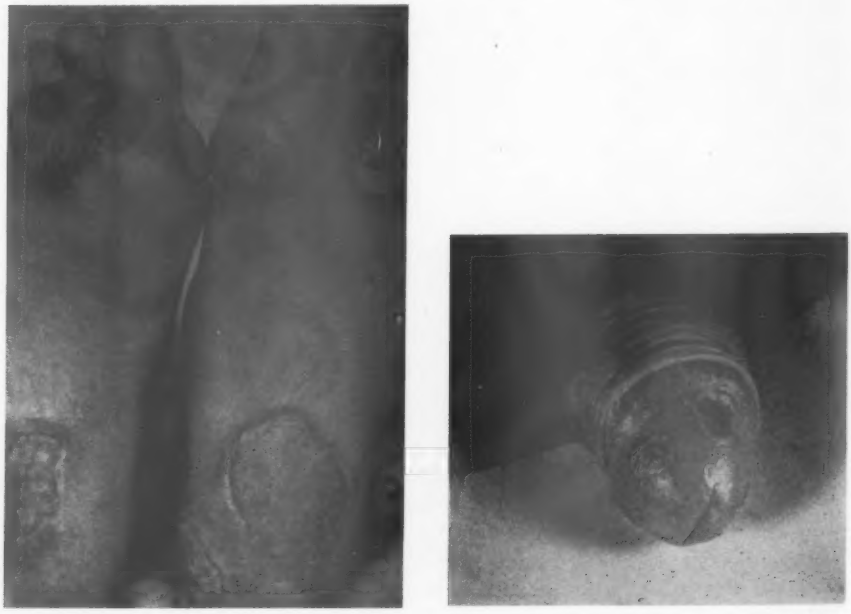
Fig. 4.—Lipoid proteinosis. The patient has numerous extensive yellowish infiltrates in lips, tongue, and buccal and pharyngeal mucosa; he has been unable to speak above a whisper since birth. The tongue is firm and bound down to the floor of the mouth; it cannot be protruded beyond the lips.

mouth by a dense yellow-gray infiltrate so that it cannot be protruded beyond the lips. The lingual frenum is commonly infiltrated. The lingual papillae are often atrophic, and the dorsum may show numerous yellowish streaks. The lower lip is usually infiltrated and may be somewhat enlarged and firm. Commonly, yellowish plaques are seen on the buccal mucosa, palate, uvula, fauces, and oral pharynx. In several cases there have been dental anomalies. Teeth, commonly the maxillary lateral incisors, have been either missing or hypoplastic. Occasionally dental aplasia is marked.

Dermal infiltration is usually seen over the extension surfaces of the elbows, knees, or fingers. Axillary plaques have been noted. Waxy excrescences are seen strung along the eyelids like beaded pearls. (See Figs. 3 and 4.)

Microscopically, there is a lipoid infiltrate about the blood vessels of the corium. The lipid, apparently a phospholipid, lies loose and not within phagocytes. Laboratory findings may be normal or there may be an associated diabetes, elevation in alpha and beta globulins, and increased urinary excretion of tyrosine.

Fig. 5.—Reiter's syndrome. Marked fusiform swelling of digit is quite apparent. Arthritis may involve any joint.



A. *B.*

Fig. 6.—Reiter's syndrome. The skin lesions, keratodermia blennorrhagica, occur commonly on the soles of the feet and on the glans penis. The microscopic picture is quite similar to that seen in gonorrhea and pustular psoriasis.

REITER'S SYNDROME

Reiter's syndrome[17-19] is a symptom triad consisting of (1) arthritis, (2) conjunctivitis, and (3) urethritis. In addition, there are dermal and oral mucosal lesions, which concern us here.

The arthritis is usually multiple and transient, but ankylosis of the affected joint never occurs. The disease is self-limiting, usually resolving within six months, but recurrences are not uncommon.

A.

B.

Fig. 7.—Reiter's syndrome. Oral mucosal lesions are nonspecific, resembling very superficial aphthous lesions. The histopathology is not characteristic. The tongue is commonly involved; the labial and gingival mucosae are less often affected.

The symptom complex suggests gonorrhea, but smears of the urethral discharge are always negative for *Neisseria*. The skin and mucosal lesions (keratodermia blennorrhagica) are also similar to those seen in gonorrhea. The infiltrate is banal and not diagnostic.

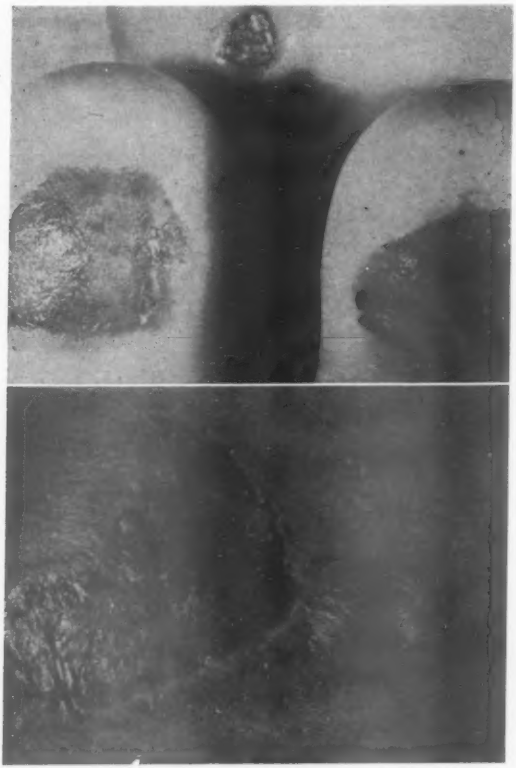
We have observed four cases, all with oral lesions. The tongue had dorsal ulceration in four cases, with labial and gingival involvement in two instances. (See Figs. 5, 6, and 7.)

EPIDERMOLYSIS BULLOSA (GOLDSCHEIDER'S AND WEBER-COCKAYNE'S SYNDROMES)

Epidermolysis bullosa was considered a rare disease prior to World War II, but screening of a large segment of the population indicated that it was more common than supposed.

The disease is primarily a hereditary one. About one-half of the cases are congenital, with a slight preponderance of male patients.

A.



B.

Fig. 8.—Epidermolysis bullosa. Note superficial ulceration of knees and umbilicus *(A)*. A small unbroken blister may be observed adjacent to an ulcerated surface *(B)*.

There are two general clinical types of the disease, the simple and the dystrophic. The simple type is divided on the basis of the extent of involvement—for example, feet only, hands and feet, or generalized. The dystrophic type is divided into *dominant* and *recessive* types, which differ in severity of manifestations.[20-24]

In the simple type (Weber-Cockayne's syndrome) there are symmetrical lesions at sites of trauma and pressure. Most commonly involved are the hands,

wrists, elbows, knees, feet, etc. The vesicles eventually rupture and heal without scarring, leaving only temporarily pigmented areas. There are no sequelae of permanent changes in skin, mucous membrane, nails, hair, or teeth. (See Fig. 8.)

In the dystrophic type (Goldscheider's syndrome), the teeth may be markedly rudimentary, hypoplastic, or congenitally absent. Partial or complete alopecia may be present, and the nails may be deformed or absent. The similarity to "hereditary ectodermal defect" should be noted. The vesicles are frequently

Fig. 9.

Fig. 10.

Fig. 9.—Epidermolysis bullosa. Note dystrophic changes in all the fingernails.

Fig. 10.—Epidermolysis bullosa. Negative pressure from nursing produced palatal bullae which ruptured, leaving large raw surfaces.

hemorrhagic, and they rupture with ulcer formation. Healing occurs under thin atrophic scars. Oral bullae, erosions, and hyperkeratotic plaques are common, especially on the tongue and buccal mucosa. Vesicles have also been reported on the lips, gingivae, and palate. These are more common in the suckling infant. Recurrent involvement has led to the binding-down of the tongue to the oral floor, and repeated lesions of the buccal mucosa produce microstomia. This

was so marked in one patient under our observation that oral examination was virtually impossible. It has been estimated that oral lesions are involved in about 16 per cent of cases of the dystrophic type. The recessive form produces lesions that are more severe. In these cases, physical and mental retardation are not uncommonly observed. (See Figs. 9 and 10.)

Squamous-cell cancer may be a complicating factor. Apparently, the changes wrought by the disease process predispose the patient to carcinomatous change. Klausner,[25] in 1913, reported the case of a 25-year-old woman in whom carcinoma developed at the site of oral lesions. We observed one patient, a 30-year-old man, whose left arm had been amputated when he was 20 years of age due to the development of squamous-cell cancer in an area of involved skin.

BONNEVIE-ULLRICH-TURNER'S SYNDROME

Bonnevie-Ullrich-Turner's syndrome[26-37] has a large complex of components. Among them are lymphangiectatic tumefaction of the hands and feet, webbed neck (pterygium colli), hypoplasia of muscles and abnormal insertion, loose skin, syndactylia, clubfoot, ovarian agenesis (Turner's syndrome), retardation of growth and sexual function, increased joint mobility, cubitus valgus (alteration in the carrying angle of the arm), mental retardation, and cranial nerve abnormalities.

In addition, there is an abnormally high palatal vault as well as underdevelopment of the mandible (micrognathia). Many patients have the genitals of one sex, while the buccal smear shows them to be of the opposite sex.[36-37]

The disease frequently goes undetected until puberty, at which time the sexual infantilism is noted as an indication of gonadal deficiency. (See Figs. 11, 12, and 13.)

Laboratory findings indicate increased urinary gonadotropins, and roentgenograms show delayed skeletal maturation and epiphyseal closure.

Possibly the most constant factor is the webbing of the neck. It should be pointed out, however, that one may have webbing without the rest of the syndrome and that about 50 per cent of the cases with ovarian agenesis occur without webbing.

High palatal vault is also seen in Marfan's syndrome.[38-39] This unusual complex consists of arachnodactyly, displacement of the lens of the eye, congenital cardiac defects, etc.

OSLER-RENDÚ-PARKES WEBER'S SYNDROME

This peculiar familial disorder is known by several names, principally multiple hereditary telangiectasia and hereditary hemorrhagic angiomatosis. The literature records over 250 families affected by this disorder.[40-44] Of particular interest to the reader should be a report of the reunion of such a family.[43]

The disease appears to be of the simple mendelian autosomal dominant type. There is no sex preference, and it can be transmitted by either sex. Usually, the initial manifestation of the disease is epistaxis, melena, hematuria, or cerebral accident. Macular angiomas appear principally about the lips or anterior

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 11.—Bonnevie-Ullrich-Turner's syndrome. Note penile anomaly and marked lymphangiectatic edema of feet.

Fig. 12.—Bonnevie-Ullrich-Turner's syndrome. Note pterygium colli, a loose fold of skin extending from the mastoid to the acromion process bilaterally.

Fig. 13.—Bonnevie-Ullrich-Turner's syndrome. Characteristically, these children have an exceedingly high palatal vault.

tongue at puberty, although they may appear earlier or develop during pregnancy. In addition to oral manifestations, there is frequently dermal, nasal, pharyngeal, or conjunctival involvement. Arteriovenous aneurysms of the lungs, liver, gastrointestinal tract, or bladder may complicate the clinical picture. The lesions manifest on the lips and tongue are not spiderlike. They are macular, rarely larger than 3 mm. in diameter. Clinically, they do not throb to the touch, but when they bleed the hemorrhage is profuse and pulsatile. (See Fig. 14.)

Fig. 14.—Multiple hereditary telangiectasia. Note punctate macular hemorrhagic areas on lips and tongue.

SUMMARY AND CONCLUSIONS

Certainly, a large number of systemic diseases have oral components. Only a few of them have been surveyed in this article. Pindborg,[45] in a recent communication, listed seventy-four separate syndromes of dental interest—and even this list is not complete! This demonstrates the immensely wide field that exists for future investigation by those interested in oral disease. Hospitals for the chronically ill, institutions for mental and epileptic patients, and dermatology and endocrinology services of major hospitals are neglected areas of liaison for dental divisions to foster. Much mutual gain can be realized from a cooperative venture of this sort.

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CARCINOMA OF THE ANTRUM

A Clinical and Histopathologic Study

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THIS study is based on sixty-one cases of primary carcinoma of the antrum admitted to University Hospital, University of Minnesota, from 1943 to 1956, inclusive. Since the disease spreads rapidly from one paranasal sinus to another, it is not always possible to determine the exact site of origin. This is especially true in advanced cases. The clinical history, postoperative surgical notes, and the impressions of the radiologists were relied upon to select only those cases which were considered to have their primary origin in the maxillary antrum. Cases in which there was sufficient evidence of secondary involvement of the sinus from the mouth, nasal cavity, or other sinuses were eliminated. Histologic material, available in fifty-four cases, was reviewed. In the other seven cases, diagnosis at the time of admission was made from microscopic examination but the slides were not available for review.

Malignant disease of the antrum is quite uncommon. Malignant tumors of the paranasal sinuses comprise about 0.2 per cent of all human cancers.[1, 2] Eighty per cent of these lesions arise in the maxillary antrum.[3]

No causative factors are known for this disease. Chronic sinusitis, polyposis, and acute trauma have been implicated without any substantial evidence. There are also on record cases in which cancer developed in long-standing draining antro-oral fistulas.[4, 5]

Carcinoma of the maxillary antrum is approximately twice as common in men. Of the sixty-one cases reported here, forty-three were in men and eighteen were in women. There was a slightly higher, but insignificant, incidence of involvement of the right antrum (thirty-six cases as compared with twenty-five cases in the left antrum). Bilateral involvement of the sinuses from independent lesions has been reported, but no such case was encountered in the present series.[6] The youngest patient was 22 years old, and the oldest was 85 years. The average age was 64 years. Nearly 95 per cent of the patients were over 40 years of age, and 82 per cent were in their sixth to eighth decades (Chart 1). Thus, carcinoma of the antrum is primarily a disease of relatively

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advanced age. The average lapse of time between the onset of symptoms and the establishment of diagnosis was only five to eight months.

For the purposes of this study, the most important signs and symptoms of carcinoma may be divided into five main groups.

Group I includes oral symptoms, such as unexplained localized or referred pain in the upper premolar or molar teeth. This may be due to pressure or to actual involvement of the posterior superior dental nerve by the malignant process. The next most common sign may be loosening of teeth or alteration

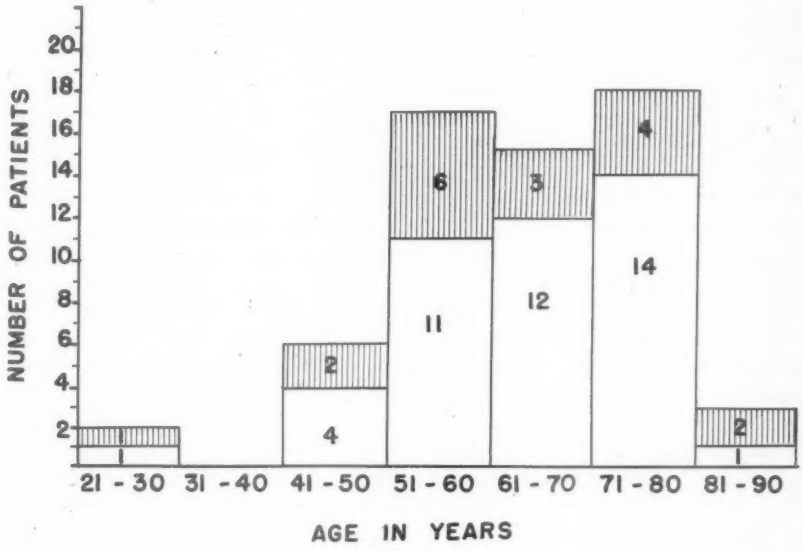

Chart 1.

in their alignment. Other symptoms referable to the oral cavity may be swelling of the palate, the alveolar ridge, or the gingivobuccal sulcus, causing difficulty in the wearing of dentures. The swelling has been most commonly confused with dental abcess or dental cyst. Following extraction of loose or aching teeth, the sockets fail to heal or there may develop, independently, an antro-oral fistula through which neoplastic tissue usually protrudes. The above-mentioned signs and symptoms arise when the neoplasm originates in the floor of the antrum. Trismus may result from extension of the tumor into the pterygoid fossa through the infratemporal surface of the antrum.

According to Larsson and Mortensson,[7] oral subjective symptoms occurred in 26 per cent of their cases and represented the first symptom observed by the patient in 15 per cent.

Group II constitutes nasal symptoms which, in order of their frequency, are (a) unilateral nasal stuffiness, (b) unilateral nasal discharge, ranging from clear and watery to foul and yellow or occasionally blood-tinged, and (c)

chronic epistaxis. Nasal obstruction may impart a "nasal tone" to the voice. A tumor mass protruding into the nasal cavity may often be seen. These symptoms are caused by cancer originating in the medial wall or by its extension from other parts of the antrum.

Group III is composed of ocular signs or symptoms resulting from the involvement of the floor of the orbit. These are characterized by puffiness of the eyelids, unilateral tearing from lacrimal gland involvement, failing vision, diplopia, and proptosis.

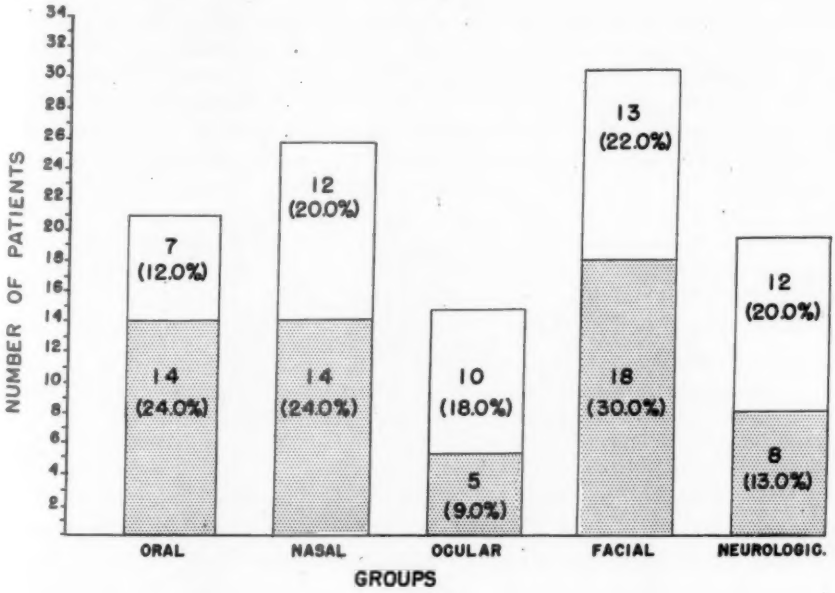

Chart 2.

Group IV includes facial symptoms resulting from the involvement of the anterior wall of the antrum. These are characterized by marked swelling of the cheek, causing facial asymmetry and disfigurement. The neoplasm may erode through the bone into the skin. In advanced cases, there may be ulceration and formation of an antro-facial fistula. Due to invasion of the infra-orbital nerve, numbness or paresthesia of the skin of the cheek is not an uncommon symptom.

Group V includes all neurological symptoms except toothache and numbness or paresthesia of the skin of the cheek. These neurological symptoms are due to involvement of the seventh and eighth nerves and meninges. There may be unilateral deafness, unilateral facial paralysis, and even hemiplegia. Also included in this group are generalized headache and localized and referred pain to the frontal, temporal, parietal, or occipital regions.

Detailed history was available in only fifty-nine patients. Chart 2 shows the distribution of patients into different groups on the basis of their initial and subsequent symptoms. It is quite evident from this that facial symptoms are most common. Next in order of frequency are nasal, oral, neurological, and ocular symptoms. Facial symptoms were present in thirty-one patients (52 per cent) and represented the initial symptoms in eighteen patients (30 per cent). Swelling around the nose, eye, and cheek was the predominant feature of this group. Paresthesia of the cheek was the initial symptom in two patients and developed subsequently in another two cases. Nasal symptoms occurred in twenty-six patients (44 per cent) and represented the first symptoms in fourteen patients (24 per cent). Nasal obstruction was the chief initial complaint. Twenty-one patients (36 per cent) comprised the oral group. Fourteen patients (24 per cent) noted first symptoms in their dental apparatus. Toothache of unexplained origin was the most common complaint. In the ocular group only five patients (9 per cent) presented themselves initially with eye symptoms, and another ten patients developed such symptoms subsequently. Lacrimation was the most common symptom. In the neurological group there was a total of fourteen patients (24 per cent). In eight patients (14 per cent) the initial symptom was either localized pain in the region of the maxilla, referred pain to the occipital, frontal, or parietal region, or generalized headache. One patient developed hemiplegia, and another developed unilateral deafness during the course of the disease.

Carcinoma of the paranasal sinuses may spread through lymphatics or/and through the blood stream. A varied incidence of metastases has been reported in the literature. The proponents of a general belief that metastases are uncommon in antral malignancy attribute this low incidence to rapid spread of the disease to the surrounding vital structures, producing fatal complications.[3, 8] This is not borne out by reports published by other investigators.[9-11] Ringertz,[9] reporting the largest series of cases from his collection, found the total incidence of metastases to be as high as 38.9 ± 3.3 per cent. Similarly, Windeyer[10] found glandular metastases in 32.7 per cent of 153 cases and generalized metastases in 9 per cent.

Among sixty patients in the present series there was clinical, roentgenologic, or microscopic evidence of metastases in only thirteen patients (22 per cent). In ten patients (16 per cent) there was clinical evidence of lymph node involvement, and in eight of these it was confirmed microscopically. In four patients (7 per cent) there was evidence of generalized metastases to the lungs, and two of these at necropsy revealed spread to the bones, brain, and liver. We agree with Tabb[5] that the incidence of metastases is higher than generally reported due to the facts that (1) many patients die early from local extension before clinical evidence is easily discernible, (2) lymph vessels drain first to the retropharyngeal lymph nodes which because of their location, are not easily palpable, and (3) only a small proportion of the patients are subjected to necropsy.

Larsson and Mortensson[7] pointed out a pronounced correlation between the degree of oral involvement and the incidence of lymph node metastases.

They found that incidence of lymph node metastases increased from 17 per cent to 38 per cent when the tumor had ulcerated into the oral cavity. They attributed this to the difference between the lymphatic drainage in the paranasal sinuses and in the oral cavity. It has been generally observed that oral carcinoma shows a higher frequency of lymph node metastases than antral carcinoma. When a paranasal carcinoma has invaded the oral cavity, it probably behaves like an oral carcinoma with regard to its metastasizing properties.

An early diagnosis of carcinoma of the maxillary antrum is difficult, since the tumor remains asymptomatic as long as it grows from the antral mucosa into the antral cavity. It is in the late stages, when the surrounding bony walls are invaded by the neoplasm, that symptoms become apparent. Furthermore, carcinoma of the antrum is frequently associated with secondary infection of the sinus and the symptoms simulate sinusitis, masking the true nature of the disease. Roentgenologically, early antral carcinoma may show only clouding of the sinus which, in itself, is not diagnostic of the disease (Fig. 1).

Fig. 1.—Roentgenogram showing early carcinoma of the antrum. Note the radiopacity of the left antrum, with minimal distortion of its bony walls.

It is only in the advanced case that bone destruction becomes apparent and, if one rules out osteomyelitis, it is largely pathognomonic of malignancy (Figs. 2 and 3). In the present series, roentgenograms were available in forty-two cases. Each case showed cloudiness, and thirty-seven (88 per cent) exhibited destruction of one or more bony walls of the antrum.

Differential diagnosis of the diseases of the antrum would include chronic sinusitis, specific infections, cysts, and benign and malignant tumors.

Chronic sinusitis is more likely to be bilateral; it seldom causes tumefaction; and it is amenable to conservative measures.

Specific infections, such as tuberculosis and syphilis, are seldom primary in the antrum. A thorough medical history and serologic tests may aid in diagnosis.

Fig. 2.—Roentgenogram of an advanced carcinoma of the antrum showing radiopacity, expansion, and destruction of the bony walls of the right maxillary antrum.

Nonsecreting cysts are diagnosed roentgenographically. They present a smooth, dome-shaped tumefaction in the antral cavity without involvement of the bony walls. Retention cysts, on the other hand, progressively increase in size and may even cause resorption of the walls of the sinus due to pressure rather than invasion.

Dentigerous cysts usually exhibit partially or fully formed teeth. Benign tumors, such as ameloblastoma, are most common in patients between 30 and 40 years of age. When polycystic, the ameloblastoma has a characteristic honeycombed roentgenographic appearance. Giant-cell reparative granuloma occurs most commonly in the second decade. Furthermore, benign tumors follow a long-protracted course, are usually painless, and seldom cause paresthesia. Malignant tumors, such as Ewing's sarcoma and osteogenic sarcoma, also occur most commonly in the first and second decades, but they are more rapid in their course and may involve the nerves, causing pain, paresthesia, or numbness.

A definitive diagnosis of carcinoma of the antrum is always established by microscopic examination. Aspiration biopsy is of value only when it is

positive; it is of no use when it is negative. The Papanicolaou technique is useful only when the tumor mass is protruding through the nasal or oral cavity. The most widely accepted technique is the incisional biopsy through a Caldwell-Luc approach or through the nasal cavity.

The maxillary antrum is lined by pseudostratified, ciliated, columnar epithelium. This epithelium readily undergoes metaplasia to the squamous

Fig. 3.—Roentgenogram of a very advanced carcinoma of the antrum with involvement of the surrounding soft tissues. Note the complete destruction of the boundaries of the left maxillary antrum.

variety, and therefore a vast majority of malignant tumors arising in this location are of the squamous-cell carcinoma type. Another possibility is that squamous-cell carcinoma may arise directly from misplaced epithelial rests which are not uncommonly found in the region of the paranasal sinuses. It also has been noted that the respiratory epithelium may be transformed into transitional-cell epithelium similar to that seen in the urinary tract. The malignant neoplasm arising from such epithelium in the antrum has been named transitional-cell carcinoma. We prefer the term "noncornifying squamous-cell carcinoma." When well-differentiated, it is composed of solid sheets of epithelial cells, which are uniform in size and shape with an occasional mitotic figure (Fig. 4). In the anaplastic variety the cells vary in size and shape, with scant cytoplasm and homogenous blue-staining nuclei. They may be scattered singly, or they may form small nests. Occasionally, these cells assume sarcomatoid appearance, but their transition from epithelial cells can

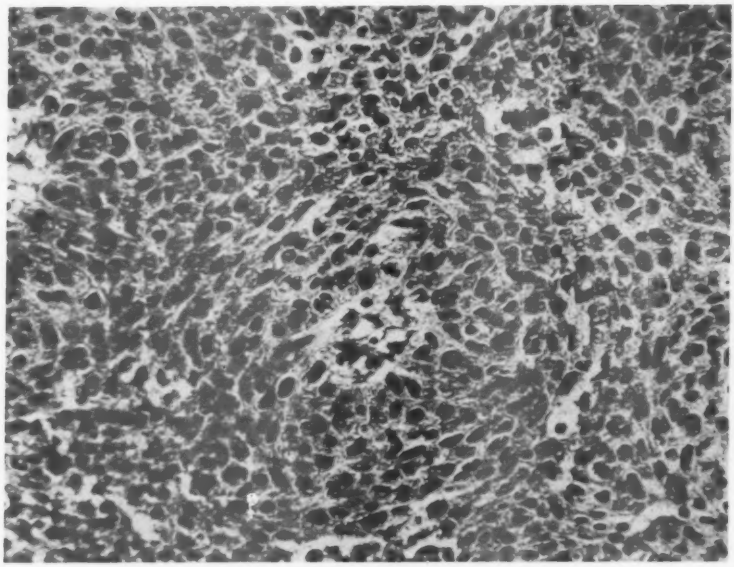

Fig. 4.—Photomicrograph of a well-differentiated, noncornifying, squamous-cell carcinoma. The cells are uniform in size and shape, with relatively few mitoses.

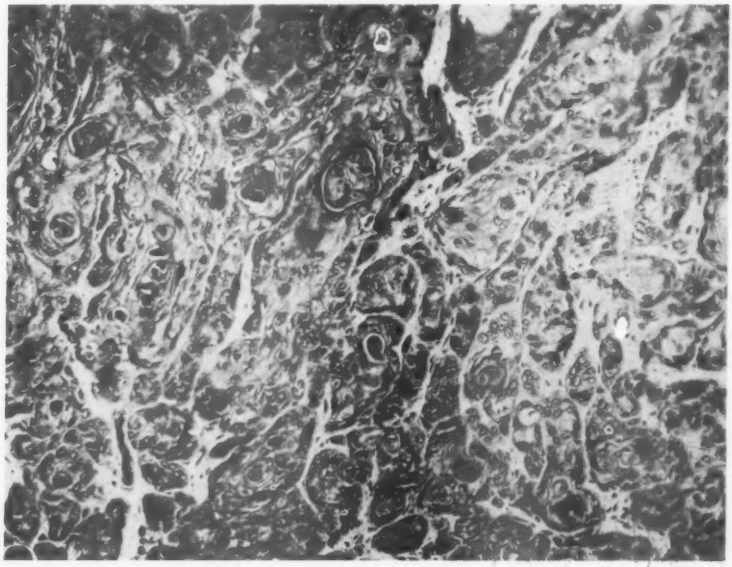

Fig. 5.—Photomicrograph showing cornifying squamous-cell carcinoma with formation of epithelial pearls.

be traced in different sections of the same specimen. When mixed with an abundant lymphocytic infiltration, such anaplastic neoplasms have been referred to as lymphoepithelioma.

Cornifying squamous-cell carcinoma also may exhibit all degrees of malignancy. Keratinization may be in the form of epithelial pearls (Fig. 5), or it may be present only in individual cells.

Both cornifying and noncornifying varieties have together been called epidermoid carcinoma, and at times they exhibit a papillary arrangement of cells spoken of as papillary carcinoma (Fig. 6). Geschickter and Copeland[12] and Pfahler and Vastine[13] consider the origin of papillary carcinoma to be benign papilloma.

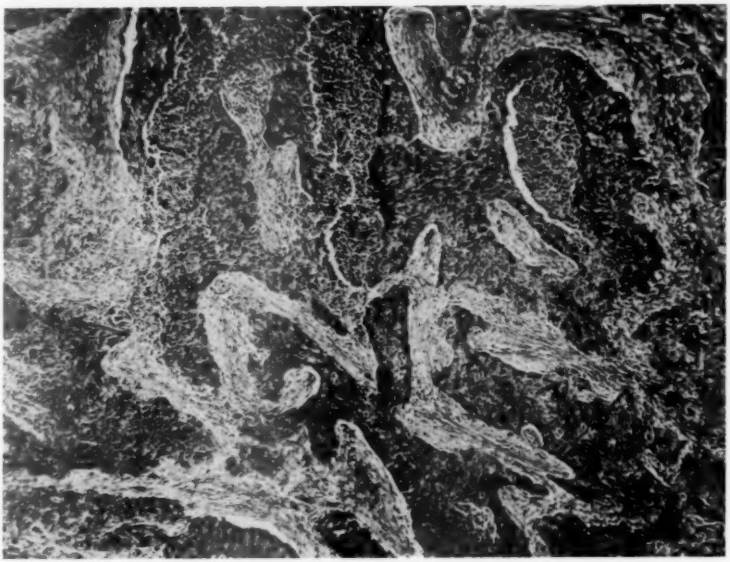

Fig. 6.—Photomicrograph of a papillary type of epidermoid carcinoma.

The lamina propria of the antral lining contains mucous glands. The most common type of adenocarcinoma arising from these glands, in this location, is cylindroma (Fig. 7). Basal cells with deeply pigmented nuclei and little cytoplasm form glandlike structures which are separated from each other by hyalinized collagenous connective tissue.

There were fifty cases of epidermoid carcinoma, varying from well-differentiated to anaplastic types, and only two cases of cylindroma in the present series.

A detailed discussion of the treatment of carcinoma of the maxillary antrum is beyond the scope of this article. It may suffice to say that combinations of radical surgery and irradiation have proved to be more effective than

either surgery or irradiation alone. Surgery alone is inadequate in many of these cases, since the extension of the tumor to areas not resectable is common. Surgery is essential, however, for the establishment of drainage of the sinus which is almost always secondarily infected in this disease. Irradiation alone has certain disadvantages. Cancer-lethal doses of irradiation may be followed by such complications as pansinusitis, infection of bone with sequestration, and ocular edema. If the bone is invaded by the neoplasm, it is difficult to eradicate cancer with radiation without producing radio-osteonecrosis.

Fig. 7.—Pseudoadenomatous basal-cell carcinoma (cylindroma). Note uniform basal cells with deeply staining nuclei and scant cytoplasm forming glandlike spaces separated from each other by collagenous connective tissue.

In the present series of fifty-nine treated patients, thirty were treated with irradiation alone, eight with radical surgery, and twenty-one with radical surgery followed by irradiation. It may be stated that in most of the cases, radiation alone was used because surgery was contraindicated because of advanced age, poor general health, extension of the tumor to the base of the skull, pterygoid fossa, or skin, or generalized metastasis.

There was a follow-up in fifty-two cases. Thirty-five patients died from the disease, and three died from postoperative complications, such as pulmonary embolism. The average span of life after the diagnosis of the disease, recorded in twenty-nine patients, was only twelve months. Of the remaining fourteen patients, six were followed for less than three years and then were lost. Thus, only eight patients survived for three years, and only five completed a five-year survival period. In other words, the five-year survival rate

is 10 per cent, and the three-year survival rate is 15 per cent in the present series. This survival rate is in close agreement with the rates of 9.5 to 14 per cent reported by Houser[14] (9.5 per cent), Cranmer[15] (14.0 per cent), Martin[2] (13.0 per cent), and Mattick and Streuter[11] (10.3 per cent), but it is at variance with the findings of Hara[17] and New,[16] who claimed five-year survival rates of 33.3 per cent and 40.0 per cent, respectively. This discrepancy could be due to the following factors:

1. Patients in the present series were mostly in an advanced stage of the disease, and the treatment was more of a palliative than a curative nature. Hara showed that in his series the five-year cure rate varied from 33.3 per cent to 6.6 per cent in a group of patients with early disease as compared to a group with advanced disease.

2. The present study was exclusively limited to primary carcinoma of the antrum. Secondary neoplasms involving the antrum were not taken into account.

DISCUSSION

The number of cases at our disposal is small, and the variables involved are so numerous that no correlation could be established between the prognosis of the disease on the one hand and the type and degree of malignancy, the location, the regional and distant metastases, and the methods of treatment employed on the other.

It is, however, a well-accepted fact that the more anaplastic a neoplasm is, the more destructive it is locally and the faster it is likely to metastasize. This is true of malignant neoplasms of the maxillary antrum as well as those of other sites. This has been demonstrated by Larsson and Mortensson, who showed that in their series the poorly differentiated carcinomas showed the highest incidence of metastases and the poorest prognosis. The site of origin of carcinoma in the maxillary sinus plays a critical role in the prognosis of the disease. The neoplasms originating in the superior, medial or posterior wall offer much more serious prognosis than those that originate in the inferior or anterior walls of the sinus. This is due to the fact that tumors originating in the former sites spread readily to the orbit, the ethmoid sinuses, the nasal cavity, and the meninges. Furthermore, the treatment is unsatisfactory due to inaccessibility. According to Larsson and Mortensson, the spread of the disease to lymph nodes markedly decreases the survival rate. In their series, the five-year survival rate dropped from 29 per cent in those without lymph node involvement to 7.5 per cent in the cases with lymph node metastases. The mode of treatment seems to have significant effect on the prognosis of the disease. Schall,[18] in 1943, found that surgery combined with radiation offered a better than two-to-one chance for five-year survival as compared with irradiation alone. This finding has been substantiated by several other investigators.[7, 19]

In addition, there are other factors which are peculiar to the behavior of malignant neoplasms of the maxillary antrum and which have a bearing on the

prognosis of the disease. Carcinoma of the maxillary antrum strikes relatively older persons; it attains a considerable size and causes extensive destruction before it produces symptoms, thus delaying early diagnosis. Furthermore, extension of the disease to the surrounding vital structures and the inaccessibility for treatment are additional factors which contribute to such a grave prognosis. Except for an early diagnosis and an improvement in the methods of treatment, all other factors are beyond control. The following suggestions may help in the establishment of an early diagnosis of antral malignancy:

1. Dental pain, localized or referred, and looseness of teeth without apparent cause should be thoroughly investigated before teeth are extracted. Extraction of teeth opens pathways so that the tumor can spread through the socket into the oral cavity.

2. A chronic refractory sinusitis, repeated unilateral stuffiness, and epistaxis in patients over 40 years of age should be suggestive of underlying malignancy.

3. When the patient has a noninflammatory, firm swelling of the cheek and unexplained headaches, the possibility of antral malignancy should be considered in the differential diagnosis.

4. Polyps from the nose and antrum should be removed and subjected routinely to microscopic examination.

5. An exploratory procedure by qualified dentists in suspicious cases should be encouraged.

SUMMARY

1. Carcinoma of the maxillary antrum is twice as common in men as in women. The highest incidence is in the sixth to eighth decades of life. The average age of patients in our series was 64 years.

2. The most common sign of antral malignancy is swelling around the eye, nose, and cheek. Next, in order of their frequency, are nasal, oral, neurological, and ocular symptoms.

3. In over 25 per cent of the patients, initial signs and symptoms appear in the oral cavity and may call for consultation with a dentist.

4. Due to the asymptomatic nature of the disease in its early stages, in the majority of cases diagnosis is not made until the disease is advanced. Upon admission, 88 per cent of the patients demonstrated roentgenologic evidence of destruction of one or more bony walls of the antrum.

5. Metastases are not as infrequent as is generally believed. In the present series, 17 per cent of the patients had lymph node involvement, and 7 per cent had generalized metastases.

6. There were fifty cases of epidermoid carcinoma, and only two were of the cylindroma variety.

7. Of fifty-two patients, three died of postoperative complications. Among the remaining forty-nine patients, five (10 per cent) lived for more than five years and eight (15 per cent) lived for three years.

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CAT-SCRATCH DISEASE

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CAT-SCRATCH disease (cat-scratch fever, nonbacterial regional lymphadenitis, benign lymphoreticulosis) is an infectious process, often accompanied by fever, malaise, and lymphadenitis, and usually associated with the scratch of a cat. The existence of this disease as an entity was probably first suspected by Foshay in 1932, although Debré and associates[5] published the first paper on the subject in 1950. Since that time, many cases have been reported in the literature, with the first American publication appearing in 1951.[8]

Because the disease has an excellent prognosis, it is important that it be differentiated from the many specific infections and tumors with which it has been confused clinically. Furthermore, in the cervicofacial area, cat-scratch disease may easily be mistaken for a lymph node manifestation of a nonspecific oral infection or for a sialadenitis, particularly if the infected node is in close proximity to a salivary gland.

It is our purpose to review the literature on this disease and to present four cases, all of which occurred in the cervicofacial area and posed problems in differential diagnosis.

CASE 1.—The first case was submitted to the Oral Pathology Branch of the Armed Forces Institute of Pathology in 1955. It involved a 24-year-old white man who developed a gradually increasing "tumor" in the parotid gland area over a two-month period. Since the swelling was asymptomatic, a clinical diagnosis of mixed tumor was made. However, histologic examination of the specimen ruled out this impression by revealing a nonspecific chronic granulomatous process involving the lymph node which was embedded in parotid gland tissue. Each of the larger granulomas was characterized by a well-defined collar of clear epithelioid cells surrounding a collection of neutrophils and debris, with occasional lymphocytes and plasma cells also present (Figs. 2, 3, and 4). The histologic picture was suggestive of lymphopathia venereum, tularemia, or cat-scratch disease. On further questioning of this patient, it was found that he had been scratched and bitten by his Siamese cats several times during the past year. He had received a scratch on the face about two weeks before onset of the parotid node swelling but had not noted any local or systemic symptoms during the course of the disease. A further complicating fact, volunteered by the patient, was that several years previously he had raised rabbits which he used for his own consumption, but he added that none of them had ever appeared unwell.

From the Armed Forces Institute of Pathology, Washington, D. C.

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Tuberculosis was ruled out because of the negative clinical findings and the absence of caseous necrosis and acid-fast organisms in the microscopic specimens. No bacteria or fungi were found in specially stained sections; tularemia, rickettsial diseases, syphilis, and infectious mononucleosis were considered highly improbable because of negative serologic tests. Lymphopathia venereum was ruled out on the basis of negative serologic and skin (Frei) tests. By the process of elimination, cat-scratch disease was considered to be the most likely cause of the patient's symptoms. A definite diagnosis was made when the patient developed a positive reaction to an intradermal injection of cat-scratch antigen after forty-eight hours.

This brief introduction to a previously unencountered entity stimulated our further study of the disease. At that time, the most complete review and discussion of cat-scratch disease available were those by Daniels and MacMurray.[2-4] Since that time, equally comprehensive studies and reviews have been published by Kalter, Prier, and Prier[10] and Merten.[11] Trieger[18] has reported the first case that we have seen in the dental literature.

A review of these as well as a study of many individual case histories elicited the following general information on cat-scratch disease.

Incidence.—Cat-scratch disease is worldwide, with cases being reported from the Americas, Asia, Africa, and practically all European countries. It may occur in any race and at any age, with the preponderant number occurring in children. About two-thirds of the patients are under 30 years of age, but even a few in their 70's have contracted the disease. More cases seem to occur in winter, with a peak in December. The incidence of the disease is probably much greater than it is thought to be at present.

Etiology.—Most workers feel that the disease is caused by a virus. To date, however, no virus has been demonstrated by any of the usual techniques. Mollaret and associates[12, 13] have successfully transmitted this disease from infected human lymph nodes to monkeys and to a human recipient. In all instances, the clinical disease was reproduced and the skin tests became positive, whereas formerly they were negative. Unfortunately, attempts by other investigators to reproduce these results have not been successful to date. Even though almost all of them have inferred a relationship between cat-scratch disease and those infections caused by the psittacosis-lymphopathia venereum group of viruses, Armstrong and colleagues[1] recently have performed some work which casts doubt upon this inference. These authors have confirmed the findings of the French writers regarding the presence of low-titered complement-fixing antibodies to Lygranum CF* antigen in a minority of patients with classic cat-scratch disease; however, they do not agree with the interpretation that this indicates a relationship between the virus of lymphopathia venereum and that of cat-scratch disease, since the presence of low-titered complement-fixing antibodies to Lygranum CF is also found in other diseases, particularly among older control groups not affected with the disease and with no history of an attack. They feel that low-titered reactions appear related more to the age of the patient than to the presence of cat-scratch disease.

*Commercial antigen used in serologic testing for lymphopathia venereum.

Epidemiology.—About 90 per cent of patients with cat-scratch disease have had recent contact with cats, although they have not necessarily been scratched. There is a definite history of scratches in about 55 per cent to 60 per cent of the cases. Although a small group of cases appears idiopathic in origin, it has been shown that lacerating agents other than the cat scratch have led to the disease. These include scratches by thorns and bits of metal, chicken scratches, and other miscellaneous abrasions.

The cat itself is not diseased, and no virus has been obtained from any of its tissues, including the claws. Foshay now believes that the human body itself may harbor the virus and that the cat scratch, as one of the most common skin lacerations, serves merely to provide a portal of entry. An interesting study was carried out by Gifford,[7] who tested the cat-scratch antigen among twenty-eight veterinarians, of whom seven subsequently demonstrated positive skin tests. Only one of the seven was thought to have active cat-scratch disease, and none gave an adequate history of having had the disease in the past. There were no statistically significant differences between the positive and negative groups of skin-tested veterinarians with respect to age, type and length of practice, animal contact, or inoculating trauma. A possibly important finding was that four of the seven skin-test-positive veterinarians gave prolonged reactions lasting eight to ten months. Gifford suggests that veterinarians may have constant contact or sporadic but continuing contact with the etiological agent of cat-scratch disease and this may produce an increased sensitivity in some of the more susceptible veterinarians. He adds, as an addendum, that the only city in which cat-scratch disease is endemic is in France where the National Veterinary College is located.

CLINICAL APPEARANCE

Typical Cases.—

Local lesions: Primary lesions are seen in about one-half the cases. They are usually on unclothed areas of the skin and may be any of several types—an inflamed scratch, a red papule, a furuncle-like lesion, an insect-bite-like lesion, or a small ulcer which may be scabbed or crusted.

Commonest time relationships: According to Daniels and MacMurray,[2] the time between the scratch and the appearance of primary lesions is three to seven days. There is a period of eighteen to thirty days between the appearence of the primary lesions and the onset of lymphadenopathy.

Lymphadenopathy: The average time is as mentioned above; however, the nodes may develop as late as two months after the initial scratch. They may be 1 to 5 cm. in diameter. They usually last about six weeks when untreated and then regress to normal. Several cases, however, have lasted for many months. In a few instances, the nodes are merely enlarged, nonpainful, and palpable, but most become tender and inflamed. About one-third of the involved nodes will suppurate and appear as though they would fistulate; however, this occurs only rarely. Infrequently, the nodes may become enlarged and tender, temporarily regress, and then repeat the process. Any of the nodes regional to

the scratch may be involved. The most common site is in the axilla, with the cervical area and finally the inguinal area next in order of frequency. The epitrochlear nodes are involved occasionally but always in conjunction with axillary adenopathy. There is no lymphangitis associated with the lymphadenopathy. When this lymphadenopathy occurs in the head and neck region, it may involve several groups of glands and is occasionally bilateral. The anterior and posterior chains are most often affected, and the supraclavicular, submental, submaxillary, preauricular, and occipital nodes are sometimes involved. Merten[11] speculates that when the cervical nodes are affected, since the appearance is often similar to scrofula, it is possible that cat-scratch disease may have accounted for the medieval cures of tuberculosis attributed to the "king's touch."

Regarding the lymphadenopathy, Kalter and associates[10] found that the operating surgeon usually thought that he was removing a solitary enlarged lymph node but that microscopic examination usually revealed a few conglomerate groups of moderately enlarged nodes. The gross tissue was nonspecific and varied from multiple small fragments of soft, reddish gray necrotic nodal and sinus tract tissue to encapsulated, rather firm masses averaging 2 to 5 cm. in diameter.

General manifestations: Aside from the lymphadenopathy, two-thirds of the patients have other complaints, such as malaise, anorexia, nausea, weakness, lassitude, aching, chills, and headache. They may have a low-grade fever of variable course and duration and/or a rash of either the macular or the papular type which lasts from one to two days. Absence of fever usually indicates a lack of suppuration of the lymph nodes. In a few instances, erythema nodosum and thrombocytopenic purpura accompany otherwise typical cases.

Atypical Cases.—These usually involve specific organ systems.

Neurological involvement: Paxson and McKay[14] added two more cases of neurological manifestations[6, 16, 17] of cat-scratch disease to bring the world total to fourteen reported cases. The criteria for diagnosis of neurological involvement are (1) history of cat-scratch or contact, regional lymphadenopathy, positive skin test, histology of lymph node consistent with cat-scratch disease plus sterile culture from the same node, and (2) otherwise unexplained neurological manifestations developing within six weeks after adenopathy. The disease may be sudden and severe in onset, with the development of such bizarre symptoms as coma. It is self-limited, however, with benign sequelae, and in most cases there is no residual effect. The spinal fluid is always sterile, although occasional lymphocytes are seen. In all cases of encephalitis with associated unexplained lymphadenopathy, the diagnosis of cat-scratch disease should be entertained.

Parinaud's oculoglandular syndrome[9, 11]: This consists of conjunctivitis and regional lymphadenitis, usually involving nodes associated with the parotid gland. Probably most of these cases are due to cat-scratch disease, with a very few due to syphilis, tuberculosis, or leptothrix infection. The site of inoculation is apparently the conjunctiva, which then undergoes a granulomatous type of inflammation followed by a typical local adenitis.

Oropharyngeal[11]: Several cases of angina and pharyngeal abscess, which proved to be antibiotic-resistant and in which suppurative sterile lymphadenitis followed, were tested with the skin antigen. Many were found to be positive for cat-scratch disease. It is possible that these infections may be due to airborne products of fur or excreta.

Pulmonary[15]: There is one recorded case of a pneumonia, probably caused by airborne products of cat fur or excreta.

Mesentery[11]: Many laparotomies have been performed in cases of suspected acute appendicitis, in which the appendices proved to be normal but the mesenteric lymph nodes were enlarged and inflamed. In many of these, the histopathology is consistent with cat-scratch disease and the skin test is positive. Histories are often obtained of cat contact without actual scratches. Merten[11] raises the question of the possible relationship of cat-scratch disease to the nonspecific mesenteric lymphadenitis commonly seen in children.

Pseudovenereal form[11]: Cat contact or scratches in the inguinal area can give a clinical and histologic picture of lymphopathia venereum. In skin testing, the Frei test and tests with cat-scratch antigen are necessary to differentiate between the two diseases.

Other unproved cases of possible cat-scratch disease[11]: Sporadic cases have been reported of acute thyroiditis, nonspecific urethritis, hepatosplenomegaly, and osteolytic lesions (mandible and ilium), some of which may well have been examples of cat-scratch disease.

DIAGNOSIS

The diagnosis is based on a positive intradermal skin test, a history of cat contact, and the characteristic clinical picture of the disease in which other causes of regional lymphadenopathy have been eliminated. A lymph node biopsy is not necessary for the diagnosis under these conditions, although it is valuable in atypical cases. If the biopsy has been made, however, it should be characteristic of cat-scratch disease. In the routine laboratory procedures, the total white blood count is normal or slightly elevated, the differential is normal with some cases showing a slight eosinophilia, and the sedimentation rate may be slightly increased. All cultures for bacteria are negative, serologic tests are negative except for the occasional positive Lygranum test in low dilution, and no reactions are seen on testing the cat's serum.

Intradermal Test.—This is similar to the Frei or tuberculin test in that bacteriologically sterile pus from a lymph node of a proved case of cat-scratch disease is necessary to prepare the antigen. (Although the ground-up node itself may be used, the aspirated pus seems to be better.) The aspirated material is diluted 1:5 with buffered saline at a pH of 7.4 and heated for two hours one day and one hour the next day at 60° C. It is then tested for bacteria by inoculating thioglycolate medium, blood agar, guinea pigs, and mice. No bacterial growth should be present. The antigen is then kept in 25 ml. amounts in rubber-capped sterile serum bottles. It is mandatory that antigenic materials from patients with previous histories of jaundice not be used.

An intradermal injection of 0.1 ml. is made in the forearm, and the test is read in twenty-four to forty-eight hours. A positive reaction is represented by at least a 5 mm. area of induration and/or a 10 mm. area of erythema at the site of injection. Although the reaction usually appears in one to two days, it may rarely be delayed for from six to seven days. It appears that some batches of the antigen act more rapidly than others and some retain their potency much longer. An occasional person may have a positive test but not remember having had any disease. Probably at one time these persons had only a slight case of lymphadenopathy which regressed spontaneously, was unexplained, and forgotten; however, skin sensitivity toward the antigen was imparted. The low incidence of positive tests in control groups probably indicates relatively high resistance to the virus by man. Once obtained, the sensitivity will remain for many years. Kalter and co-workers,[10] in a large series of cases, demonstrated the specificity of the test.

TABLE I. CAT-SCRATCH DISEASE—DIFFERENTIAL DIAGNOSIS

LESION	TEST FOR DIFFERENTIAL DIAGNOSIS	RESULT IN PATIENT WITH CAT-SCRATCH DISEASE
1. Neoplasms	Biopsy	Different
2. Lymphopathia venereum	Biopsy	Indistinguishable
	Frei test	Negative
	Lygranum (serologic)	May be positive in low dilution
3. Tularemia	Biopsy	Indistinguishable
	Agglutinations (specific)	Negative
4. Tuberculosis	Biopsy	Occasionally similar
	Stains	Negative
	Culture	Negative
	Tuberculin	Negative
5. Nonspecific lymphadenitis (bacterial or fungal)	Biopsy	Usually different
	Stains	Negative
	Culture	Negative
	Skin sensitivity test	Negative
6. Rickettsial diseases	Agglutinations (with members of the Proteus group)	Negative
	Biopsy	Usually different
7. Syphilis	Serologic tests	Negative
	Biopsy	Usually different
8. Infectious mononucleosis	Biopsy	Usually different
	Examination of blood smear	Negative
	Heterophil agglutination	Negative

Differential Diagnosis.—This must include tumors in the area, such as those of the parotid gland and lymphomas. Infections, such as tuberculosis, tularemia, brucellosis, lymphopathia venereum, syphilis, fungus infections, bacterial adenitis, and infectious mononucleosis, must be ruled out (Table I).

HISTOPATHOLOGY[10, 19]

Primary Skin Lesions.—These often show a superficial circumscribed ulceration with an underlying inflammatory process into the corium, consisting

of lymphocytes and neutrophils perivascularly arranged. Plasma cells and eosinophils are prominent early, and macrophages appear later. Occasionally, epithelioid and giant cells are also seen here.

Lymph Node.—Although the histology is nonspecific, Kalter and associates[10] found certain characteristics to be of value. A capsular thickening with marked chronic inflammatory cell reaction is constantly present. Occasionally, eosinophils and giant cells are seen. Varying degrees of enlargement of the cortical lymph nodules and their germinal centers are present. Transformations from the basophilic cytoplasm of the primitive reticuloendothelial cells to the eosinophilic cytoplasm of epithelioid cells are noted in these initial stages. These findings are uniform among all types of reactions. The remainder of the findings are both cortical and medullary and usually consist of one of three patterns, although some admixture is seen.

Acute Cases (Figs. 3 and 4).—These, in Kalter's[10] series, are the most common and have a "soft" tuberculoid granuloma appearance. There is a large, central, eosinophilic-staining, amorphous, caseous material about which epithelioid cells with occasional lymphocytes and giant cells are seen. The caseous foci tend to fuse with adjacent similar areas, and they frequently extend through the capsule. Acid-fast stains are negative. This type cannot be differentiated histologically from tuberculosis; therefore, many cases of cat-scratch disease in the past may have been misdiagnosed as bovine tuberculosis.

Acute Necrotizing (Fig. 2).—The center is necrotic with neutrophils demonstrating marked pyknosis and karyorrhexis. The epithelioid-cell layer surrounding the necrotic material is definitely present, although possibly not so well-defined as in the first type. Giant cells are seldom seen here. Fusion of adjacent granulomas and extension into the capsular tissue are common. In this situation, the lesions appear identical to tularemia, lymphopathia venereum, and occasionally brucellosis.

Epithelioid-Cell Type (Fig. 1).—Collections of epithelioid-cell granulomas of varying sizes showing marked tendency to fusion are seen. Individual cells are large, with vesicular nuclei, acidophilic nucleoli, and abundant cytoplasm. Occasional areas appear very similar to Boeck's sarcoid. Marked germinal center hyperplasia of the lymph nodules is seen in this type, and in rare instances it has led to confusion with giant follicular lymphoma.

In all of the types mentioned, the dilated capillaries surrounding and entering the granulomas demonstrate many neutrophils.

THERAPY

Although these lesions will usually heal spontaneously, occasionally they do fistulate and persist, causing varying degrees of discomfort to the patient. If nodes are large, it has been recommended that they be aspirated and the patient placed on broad-spectrum antibiotics. This seems to shorten the course of the disease considerably. Corticotropin in doses of 40 mg. every six hours for one week may help. Radiation was tried in one case and proved not to be helpful. Only one death has been reported, and it may or may not have been due to cat-scratch disease.

From the standpoint of the pathologist, it occurred to us that we had probably diagnosed as "nonspecific granulomatous inflammation" several cases of cat-scratch disease before the entity had been described in the literature. On reviewing thirty such cases selected at random from the files of the Armed

Fig. 1.

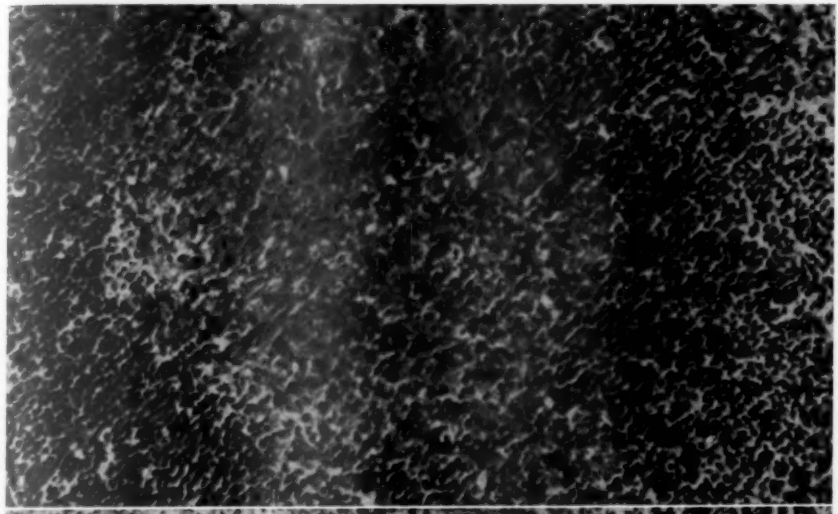
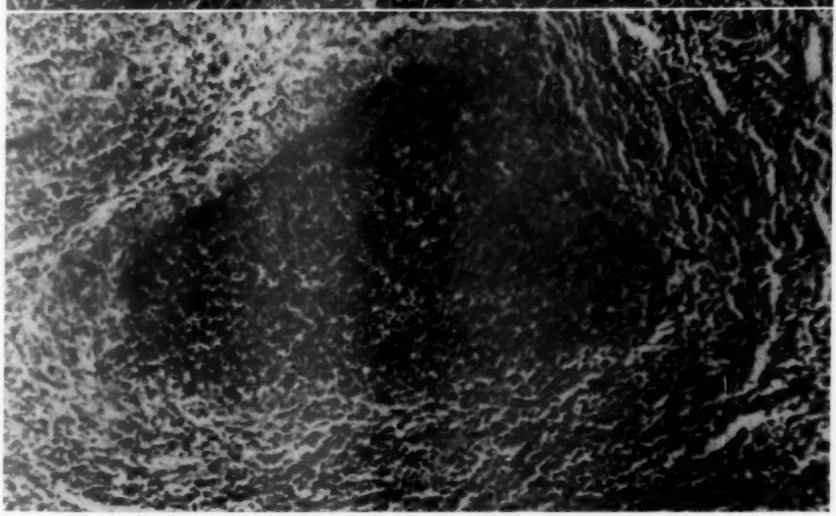


Fig. 2.



Figs. 1 and 2.—Variations in microscopic appearance of lymph nodes in cat-scratch disease.

Fig. 1.—Early change in lymph node. Granuloma composed of epithelioid cells infiltrated by neutrophils. (Magnification, ×130.)

Fig. 2.—Micro-abscess formation. Necrotic debris and neutrophils in center, epithelioid cells forming collar. (Magnification, ×130.)

Forces Institute of Pathology, we found that in five of them the history and histologic picture were consistent with cat-scratch disease. Of course, it is impossible to know at this time how many of the five suspicious cases had truly been cat-scratch disease.

Fig. 3.

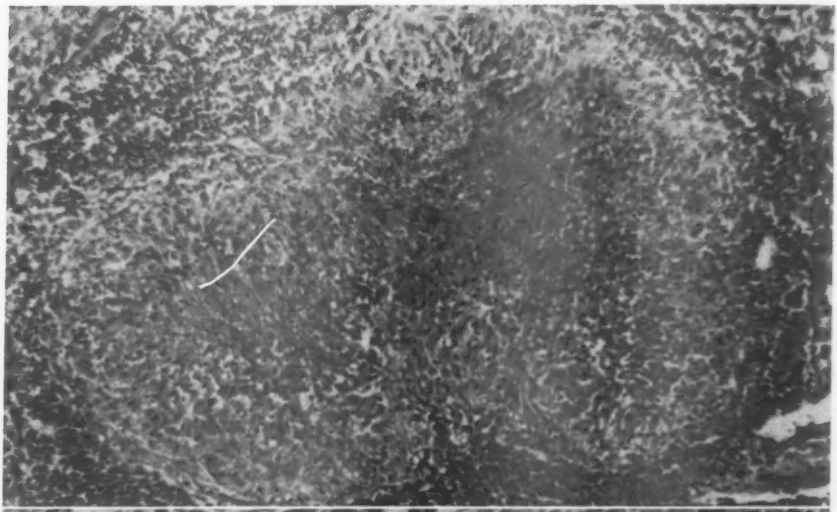
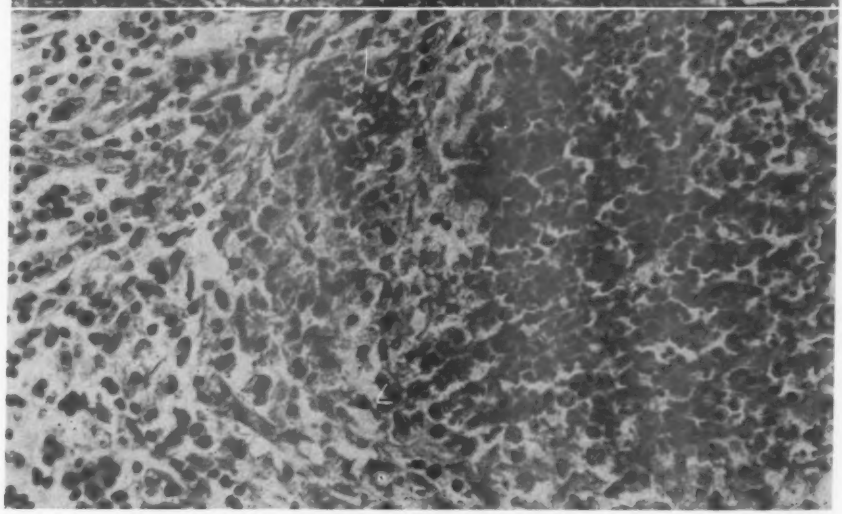


Fig. 4.



Figs. 3 and 4.—Variations in microscopic appearance of lymph nodes in cat-scratch disease.

Fig. 3.—"Tuberculoid" granuloma. Central "caseous" necrosis with epithelioid cell collar. Lymphocytes and plasma cells at periphery. (Magnification, ×130.)

Fig. 4.—Periphery of collar composed of epithelioid cells and one giant cell. Lymphocytes, plasma cells, and capillaries surround the collar. (Magnification, ×250.)

CASE REPORTS

It might be well to review three additional cases of cat-scratch disease with which we are familiar.

CASE 2.*—The patient, a 15-year-old white girl (Figs. 5 and 6), was well until about Dec. 1, 1951, when she caught a cold which persisted for about a week and then seemed to subside. About Dec. 15, 1951, she noted a few submaxillary nodules which seemed to regress and then flare up again. Local symptomatic treatment with ice bags did no good, and the patient complained that the nodes were moderately painful. An osteopath was consulted, and during the following three weeks the patient was treated with penicillin, sulfa drugs, and Aureomycin, with no observable clinical benefit. The patient had a temperature of about 100° F. for just the first two weeks after the onset of her lymphadenopathy. In February, 1952, she consulted a physician, who found a painful bilateral anterior cervical lymphadenopathy, with the left side being more in evidence than the right. There was an extension of the lymphadenopathy on the left side behind the sternocleidomastoid muscle down to the clavicle, also involving the axillary nodes. These extensive swellings were firm and fixed, not fluctuant, and slightly painful. The tentative diagnosis at the initial examination was either an infectious lymphadenopathy, a lymphoma such as Hodgkin's disease, tuberculous lymphadenopathy, or possibly infectious mononucleosis.

Fig. 5. Fig. 6.

Figs. 5 and 6.—Clinical appearance of the cervical nodes in Case 2. (Courtesy Dr. Vinton Sneeden.)

Two weeks after this examination, skin and radiographic examinations for tuberculosis were negative and a report on the biopsy specimen indicated "granulomatous inflammation, cause undetermined." The agglutination tests for tularemia and lymphopathia venereum were negative. Further quesioning at this time revealed a history of contact with cats, with occasional scratching and biting by her own cat. In March, 1952, the lymph nodes had regressed considerably, with one node on the left side remaining fluctuant. The patient at this time was on sulfonamide treatment. One month later, or eight weeks after her initial visit to the physician, skin tests with cat-scratch antigen

*Courtesy of Dr. Vinton Sneeden, Pathologist, Emanuel Hospital, Portland, Oregon.

Fig. 7.

Fig. 8.

Figs. 7 and 8.—Enlarged posterior auricular lymph node in Case 3.

Fig. 9.

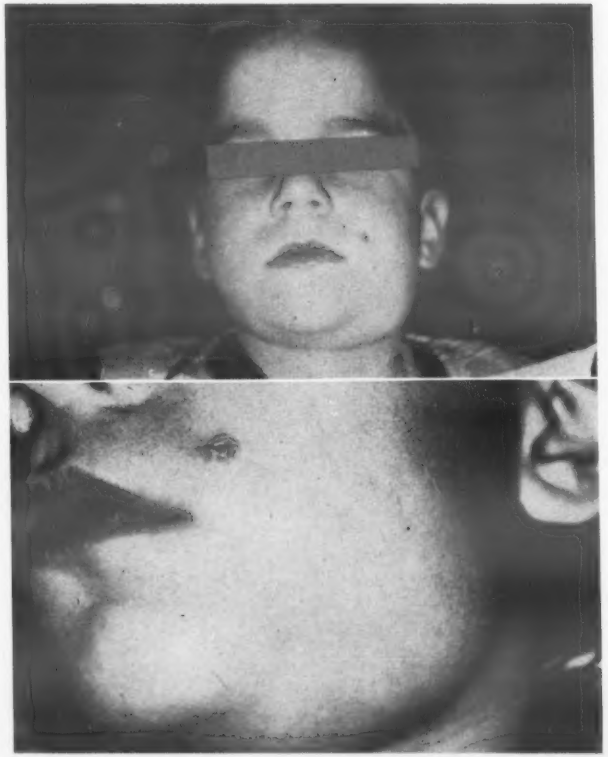


Fig. 10.

Figs. 9 and 10.—The initial lesion (scabbed papule on cheek) and the submaxillary lymphadenopathy in Case 4.

from the patient's own node and also from that supplied by Dr. Foshay were performed, and forty-eight hours later both were read as definitely positive. The only untoward sequela was drainage from one of the large lymph nodes at the angle of the left mandible which continued until April, 1952, after which evidence of healing began. There was also a small disappearing area of hypesthesia near this area of drainage under the left mandible. This appeared following the needle puncture for drainage and probably was not related directly to cat-scratch disease.

CASE 3.—This case (Figs. 7 and 8), which began in December, 1956, involved a 9-year-old white boy who developed a lymphadenopathy in the posterior auricular lymph nodes as well as in the posterior cervical chain. He had a temperature of about 100° F. for three weeks following onset of the lymphadenopathy. There was no other symptomatology, except that the one lymph node which was enlarged to almost the size of a golf ball had proved to be moderately tender. The patient's pediatrician had placed him on various chemotherapeutic agents, including sulfa drugs, penicillin, and Aureomycin, with no resulting regression of the nodes. A history of playing with neighborhood cats and cuddling them in the affected area was elicited and, therefore, a suspicion of cat-scratch disease was entertained. The patient was evaluated with regard to tuberculosis, and this was ruled out on the basis of skin testing and physical and radiologic examination. Serologic tests against the antigens of tularemia, lymphopathia venereum, brucellosis, and infectious mononucleosis were all negative, as were the agglutinations against various of the rickettsial diseases and the serologic test for syphilis. The one large node was aspirated and cultured for various bacteria and fungi, all of which proved negative. The skin test was read both twenty-four and forty-eight hours after injection and was definitely positive.

CASE 4.—The patient (Figs. 9 and 10) was a 6-year-old white boy who had been scratched by his pet cat on several areas of his body during the preceding few months. One of the spots was visible on his cheek just above the corner of his lip. Two weeks after this scratch, lymphadenopathy developed in the submaxillary area. The patient had a slightly increased temperature and malaise for two days. The skin test for cat-scratch disease was positive, while tests for the other previously mentioned infections were negative. The lesion subsided under Achromycin therapy.

SUMMARY AND CONCLUSION

In conclusion, we may state that cat-scratch disease is a regional lymphadenopathy, usually caused by a cat scratch or at least by contact with a cat, and accompanied by varying degrees of constitutional symptoms. It is likely to be seen by the general dentist and will undoubtedly be seen by oral pathologists with increasing frequency as time goes on.

Since this lymphadenopathy has an excellent prognosis, it must be differentiated from lymph node spread of intraoral infections, from specific bacterial, fungal, or viral lymphadenitis, and from neoplasms. A characteristic history and clinical course, together with a positive skin test, serve to establish the diagnosis. In atypical cases, or those in which a biopsy has been taken previously, the histology, while not pathognomonic, should be characteristic of cat-scratch disease.

ADDENDUM

Since the submission of this paper, the senior author has seen two new, previously undiagnosed cases of cat-scratch disease in children.

The authors wish to thank Dr. Marcus Horenstein for supplying the antigen and performing the skin tests in Cases 3 and 4.

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MULTIPLE MALIGNANT TUMORS INVOLVING THE ORAL MUCOSA AND THE GASTROINTESTINAL TRACT

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INTRODUCTION

In recent years the problem of multiple malignant tumors has received renewed attention. It has been noted that the oral cavity and the gastrointestinal tract are often involved by several apparently distinct and unrelated malignant tumors. These multiple sites of malignant neoplastic growth often appear simultaneously or within a short period of time. This particular problem is of considerable interest in relation to the prognosis and management of oral cancer cases. On a more academic level, the problem is of interest in that it sheds some light on the complex etiology and development of oral malignancies. We felt that further consideration of this problem was indicated, and we shall report on forty-eight cases of multiple malignancies involving the oral mucosa and the gastrointestinal tract. In thirty-six of the forty-eight cases there were multiple separate epidermoid carcinomas confined to the oral mucosa. In eighteen cases there were separate malignant tumors of the oral mucosa and other areas of the gastrointestinal tract. These cases were found in a series of 768 cases of carcinoma of the oral cavity.

REVIEW OF THE LITERATURE

Billroth[1] was one of the earliest investigators to write of multiple tumors. He applied the term to a series of similarly organized growths occurring on one tissue system and considered the tissue to be systemically conditioned to the change. Nedopil,[2] in 1877, presented the case of a 52-year-old male patient with carcinomas of the lip, tongue, and cheek. Hayward and Henderson,[3] in 1901, presented a case in which there were three separate carcinomas of the tongue in a 25-year-old woman. Richter,[4] in 1905, discussed the case of a 62-year-old man with carcinoma of the tongue as well as two esophageal foci.

The subject of multiple malignancies in general was discussed in some detail by Major,[5] Owen,[6] Neprjachin,[7] Goriainowa and Schabad,[8] and others.

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In 1932 Warren and Gates[9] presented an extensive review of the literature on multiple primary malignant tumors and evaluated a series of 1,269 cases, including forty cases of their own. They noted that multiple tumors occurred more frequently than could be explained on the basis of chance. In their study of the literature they found that multiple malignancies occurred in 1.84 per cent of cases of malignant disease. They pointed out, however, that multiple malignancies were often missed at autopsy, particularly if careful microscopic studies were not carried out. Multiple lesions in the same organ were often considered as one if the lesions coalesced and appeared as one tumor clinically. Warren and Gates found forty cases of multiple malignancies in a series of 1,078 autopsies for malignant disease and believed that this figure of 3.7 per cent was more correct. In over 1,000 cases of oral malignancy, Sarasin[10] found fifty instances in which more than one lesion occurred.

Slaughter[11] collected and classified 1,868 cases of multiple tumors from the literature, including 788 cases included in Warren and Gates's series. Thirty-nine multiple malignancies confined to the oral cavity are listed, exclusive of contiguous mucosal surfaces such as pharynx, tonsil, and esophagus. The multiple sites of oral carcinoma were as follows: tongue (twelve cases), lip (eleven cases), lip and buccal mucosa (nine cases), tongue and buccal mucosa (four cases), and gingiva and buccal mucosa (three cases). Slaughter also reviewed a series of thirty-two multiple carcinomas of the gastrointestinal tract in which one lesion involved the oral mucosa and noted involvement of tongue and stomach (six cases), tongue and pharynx (three cases), tongue and esophagus (two cases), tongue and jejunum (two cases), tongue and colon (one case), tongue and duodenum (one case), lip and stomach (five cases), lip and rectum (four cases), buccal mucosa and colon (two cases), buccal mucosa and stomach (two cases), gingiva and ileum (one case), tonsil and lip (one case), and tonsil and floor of mouth (two cases). He noted that there was a striking tendency for multiple tumors to occur in the same type of tissue—either in the same organ or in paired organs. Most multiple malignancies, as expected, were found to involve the skin. The large area of skin surface and its exposure to ultraviolet radiation could be related to the high incidence of multiple malignancies. The gastrointestinal tract was found to be involved by multiple malignancies almost as frequently as the breasts, and these two areas followed skin infrequency. Slaughter continued his studies of multiple malignancies, and his microscopic investigations led him to consider the multicentric origin of intraoral carcinoma as a reasonably common finding.[12] Epstein and Shaw,[13] in a discussion of multiple cancers in air and food passages, present individual cases involving tonsil and floor of mouth, tonsil and tongue, tonsil and epiglottis, and tonsil and pillar of fauces.

Wynder, Bross, and Feldman,[14] in a discussion of 543 male patients with cancer of the oral cavity, found that fifty-nine cases (11 per cent) had more than one primary cancer site, and 60 per cent of the patients with multiple primary cancers developed a second tumor in either the upper alimentary tract or the respiratory tract. Wynder and his co-workers found that the percentage

of heavy drinkers and heavy pipe and cigar smokers in the multiple primary cancer series was similar to that of the total oral cancer group. However, the number of patients who smoked excessively was significantly greater in the multiple series. Thirteen cases are presented in which multiple primary oral malignancies occurred within two years. The sites of these cancers are tongue and floor of mouth (three cases), tongue (two cases), tongue and palate (two cases), tongue and tonsil (three cases), lip and buccal mucosa (one case), gingiva and floor of mouth (one case), and gingiva and palate (one case). Byars and Anderson[15] reported on twenty-four cases of multiple carcinomas of the oral cavity. Ackerman and Johnson[16] investigated 206 cases of epidermoid carcinoma of the mouth at the Ellis Fischel State Cancer Hospital and found ten cases of multiple primary cancers of the mouth. The time interval was found to vary from 0 to 10 years. Ackerman and Johnson pointed out the difficulty of being certain that a second tumor was an independent lesion rather than a recurrence. They indicate certain criteria for establishing the independence of the second lesion. The longer the time elapsed, the greater is the chance of the tumor being a new one. If the tumor is on the opposite side of the oral cavity and widely separated from the original lesion, its chance of being a separate lesion is greater. Ackerman and Johnson point out that a patient with one carcinoma of the mouth has an increased chance of developing a second oral malignancy, and clinical follow-up is mandatory for the rest of his life.

PRESENT STUDY OF FORTY-EIGHT CASES

Forty-eight cases of multiple primary malignancies of the oral cavity and gastrointestinal tract were studied. This series of forty-eight lesions occurred in 768 cases of carcinoma of the oral cavity seen at Westfield State Sanatorium in Westfield, Massachusetts, from 1938 through 1958. In this series of oral cancers there were 333 lip lesions, 248 lesions of the buccal mucosa, gingiva, and floor of the mouth, 27 lesions of the palate, and 160 lesions of the tongue.

Of this series of forty-eight cases, thirty-six presented multiple, separate, and apparently distinct foci of carcinoma of the oral mucosa (Tables I and II). These patients consisted of two women and thirty-four men, ranging in age from 39 to 84 years. In this series it was noted that the time interval between lesions varied from 0 to 12 years. Of twenty-four patients in whom a positive or negative history of smoking was obtained, there were at least seven cases of heavy smoking. A history of syphilis prior to the development of oral malignancies was noted in nine cases. Following therapy, nine of thirty-six patients died as a result of the oral malignancies.

In the second group, consisting of eighteen patients, there were malignancies of the oral mucosa as well as malignant tumors elsewhere in the gastrointestinal tract (Table III). These gastrointestinal sites were the esophagus (five cases), stomach (seven cases), intestine (two cases), colon (one case), rectum (two cases), and cecum (two cases). Of these eighteen cases with oral and gastrointestinal lesions, six patients persented multiple oral lesions. Of twelve patients whose smoking habits were recorded, nine were moderately heavy smokers, using

TABLE I. MULTIPLE PRIMARY MALIGNANCIES OF MOUTH ONLY

CASE NO.	SEX	AGE	SITES							METASTASIS	SMOKING	LEUKOPLAKIA	THERAPY	OTHER LESIONS
			FLOOR OF MOUTH	BUCCAL MUCOSA	TONGUE	GINGIVA	LIP	PALATE	TONSIL					
1	F	39				xx					Cigarettes-H	x	S.	Ulcerative colitis
2	M	56	xx							x	Cigars, cigarettes-H		S.	
3	M	57			xx						Pipe, cigarettes-H		R.	Carcinoma of prostate
4	F	69		x				x			No		R.*	
5	M	66			x			x			N. R.		R.*	
6	M	47					xx				N. R.		R.	
7	M	44					xx				N. R.		R. and S.	
8	M	71	x	xx	xx					x	Pipe-H	x	R.*	
9	M	70		x				x		x	N. R.		R.*	
10	M	67					xx				Pipe	x	S. and R.	
11	M	64	x				x				N. R.	x	R.	
12	M	66		x			x				Pipe		R.	
13	M	70	x				x				Cigars		R.	
14	M	45	x				x				Cigarettes	x	S. and R.	
15	M	69	xx		xx					x	Cigarettes		R.	
16	M	55					xx				Cigarettes		S. and R.	
17	M	71					xx				Cigarettes, pipe		S. and R.	Carcinoma in maxillary sinus
18	M	55			x		xx				Cigarettes		S. and R.	Gastric ulcer
19	M	65					xx				No		S. and R.	
20	M	76					xx				N. R.		R.	Carcinoma of nose
21	M	75	x		x						N. R.		R.	
22	M	81	x		xx						Cigars, cigarettes	x	R.	Carcinoma of ear
23	M	82		x	x						Cigarettes		R.	
24	M	67		x			x				Pipe		R.	
25	M	70		xx							No			
26	M	72					xx				Cigarettes	x	R.	
27	M	72				x	x				Pipe		S. and R.	
28	M	67		x	x				x	x	N. R.		R.	
29	M	55					x		x	x	Cigarettes, pipe	x	R.	
30	M	67					xx				Cigarettes		R.	Basal carcinoma of face

* = Died.
N.R. = Not recorded.
H. = Heavy.
S. = Surgery.
R. = Radiation.

TABLE II. MULTIPLE PRIMARY MALIGNANCIES OF MOUTH AND GASTROINTESTINAL TRACT

CASE NO.	AGE	SEX	LOCATION OF ORAL PRIMARY TUMOR(S)	TREATMENT	LOCATION OF GASTROINTESTINAL TUMOR(S)	TREATMENT	SMOKING
31A	63	M	*Right tongue, floor of mouth Left tongue, floor of mouth	R.	Adenocarcinoma of rectum	R.	No
32A	66	M	*Right lower lip, commissure-left	S., R.	Carcinoma of stomach	—**	N. R.
33A	61	M	*Right lip, left lip	R.	Adenocarcinoma of stomach	S.**	Pipe
34A	84	M	*Tongue, gingiva	R.**	Carcinoma of splenic flexure	R.	Cigarettes, pipe-heavy
35A	77	M	*Maxillary gingiva, buccal mucosa-bilaterally	R., S.	Carcinoma of cecum	S.	Pipe, cigars
36A	47	M	*Soft palate, floor of mouth	R., S.	Carcinoma of esophagus	—**	Cigarettes, heavy
37A	82	M	Lower lip	S.	Carcinoma of splenic flexure	S.	Pipe, cigars
38A	66	M	Tongue, floor of mouth	S.	Adenocarcinoma of stomach	—**	Pipe
39A	68	M	Palate, uvula, tonsil	R.	Carcinoma of esophagus	S., R.**	Cigars
40A	70	M	Lip	S.	Carcinoma of esophagus	S., R.**	Pipe
41A	68	M	Buccal mucosa	R.	Adenocarcinoma of sigmoid colon	—**	N. R.
42A	69	M	Lip	S.	Adenocarcinoma of cecum	S.	Pipe
43A	51	M	Tongue	S.	Carcinoma of stomach	S.**	N. R.
44A	65	M	Lip	R.	Adenocarcinoma of stomach	—**	N. R.
45A	61	M	Tonsil, soft palate	R.	Carcinoma of esophagus	S.	Pipe
46A	67	M	Buccal mucosa	R.	Carcinoma of stomach	—**	Cigarettes
47A	71	M	Tongue, floor of mouth	R., S.	Adenocarcinoma of rectum Adenocarcinoma of stomach	S.	N. R.
48A	73	M	Buccal mucosa	R.	Carcinoma of esophagus	—**	Pipe, cigars

S. = Surgery.
R. = Radiation.
* = Multiple oral primaries.
** = Cause of death.

cigars and pipes rather than cigarettes. Syphilis was not recorded in any of these cases. All of these eighteen patients were men, ranging in age from 51 to 84 years. Mortality was very high in this group, with eleven of eighteen patients succumbing to the gastrointestinal malignancies.

CRITERIA EMPLOYED IN THIS STUDY

Cases of oral carcinoma studied were those involving the mucous membrane of the lips and oral cavity proper. In our cases of lip lesions, we considered only

TABLE III. PERCENTAGE OF MULTIPLE MALIGNANCIES

AUTHOR	YEAR	NO. MULTIPLE MALIGNANCIES	TOTAL MALIGNANCIES	PER CENT
		General		
Hanlon[17]	1931	18	710	1.9
Goriainowa and Schabad[8]	1931	23	1,238	1.8
Warren and Gates[9]	1932	40	1,078	3.7
Hurt and Broders[18]	1933	71	2,124	3.4
Bugher[20]	1934	30	983	3.1
Schreiner and Wehr[21]	1934	307	11,212	217
Burke[22]	1936	46	583	7.8
Warren and Ehrenreich[23]	1944	194	2,829	6.8
		Confined to Oral Mucosa		
Lund[19]	1933	56	1,548	3.6
Sarasin[10]	1933	50	1,000	5.0
Byars and Anderson[15]	1952	20	166	12.0
Moertel and Foss[24]	1958	64	732	8.7
Meyer and Shklar	1959	40	768	4.7

carcinoma of the mucous membrane surface of the lip and not those malignancies involving the skin surface of the lip primarily.

All the lesions considered in the study were proved malignant tumors by careful biopsy studies. The original histopathologic diagnoses and the original microscopic slides were reviewed. The oral lesions considered were all epidermoid or squamous-cell carcinoma.

To fit the criteria of multiple malignancies, all lesions considered were sufficiently separated clinically and appeared as distinct separate sites of involvement. Where the same region was involved, we accepted only those cases with carcinomas on opposite sides. Thus, on the lip and tongue we considered only bilateral lesions and omitted from our study those cases in which there appeared to be separate lesions on the same side reasonably close to one another. In these latter cases, although the lesions appeared separate and distinct, there was a reasonable possibility of extension from one site to the other. We were not able to study serial microscopic sections of many of these cases in order to rule out extension of the malignancies, so we decided not to include this type of case in our study. The lesions were separated by a sufficient amount of normal-appearing tissue. Biopsy studies revealed normal tissue at the margins in most of the cases studied.

In following the criteria of Warren and Gates,[9] we attempted to exclude the probability of one malignant tumor being a metastasis of the other. In only seven cases of our series was there clinical evidence of metastasis. Most of the lesions were well-differentiated carcinomas in which metastasis would not commonly be an early feature.

The gross and microscopic appearances of the tumors were those of the usual type of carcinoma found in these areas.

OBSERVATION

Most of the symmetrical bilateral lesions were found on the labial mucosa (eleven cases) and the tongue (five cases). In this entire series the gingiva

(and the alveolar mucosa in edentulous patients) was involved in only four cases, as compared to fifteen for the tongue, eleven for the buccal mucosa, twenty-three for the lip, twelve for the floor of the mouth, and six for the palate. We found that forty-eight of 768 cases of oral carcinoma consisted of multiple malignant sites, the other site being on the oral mucosa or elsewhere in the gastrointestinal tract. Thus, 6.25 per cent of the oral malignancies were found presenting other sites in either oral or gastrointestinal mucosa.

In the consideration of multiple malignancies confined to oral mucosa, our percentage of 4.7 is somewhat higher than that of Lund (3.6 per cent) but lower than that of Moertel and Foss (8.7 per cent). Our figure would have been somewhat higher, had our criteria for multiple sites been less severe (Table III).

GROSS EVALUATION

The largest number of these multiple oral malignancies consisted of proliferative, raised lesions. In some cases there was a papillary or verrucous character to the raised lesion. Primary ulcerations were not common, but ulcerated areas in the center of raised lesions were frequently noted. In ten cases the carcinomas developed in areas of leukoplakia which had been present for some time.

MICROSCOPIC EVALUATION

The microscopic features of these oral malignancies were consistent with those expected of carcinoma of the oral mucosa. The lesions of labial mucosa were all well-differentiated, low-grade squamous-cell carcinomas. The lesions presented varying degrees of invasion of the underlying connective tissue and occasionally of the striated muscle. In all cases the lesions formed keratin and the cellular morphology was quite regular in relation to size, shape, and chromaticity. At the invading projections of the carcinoma the connective tissue was usually densely infiltrated with chronic inflammatory cells. Bilateral lingual lesions had a tendency to present a higher degree of malignancy with deeper invasion of the underlying tissue and a notable variation in cellular morphology with the presence of bizarre mitotic figures and tumor giant cells. Two of the multiple tumor cases related to tongue terminated fatally as a result of massive local extension. Four cases of lingual carcinoma presented evidence of metastasis to regional nodes; six cases presented no evidence of metastasis. In several cases we were able to distinguish more than one focus of carcinoma arising in a large area of leukoplakia. These observations are similar to the microscopic studies of Slaughter,[12] substantiating the multicentric origin of intraoral cancer.

It is of interest that of the thirty-six patients with multiple oral primary lesions, nine died as a result of the oral malignancies; in the majority of cases the therapy was successful. In the eighteen cases with oral and gastrointestinal lesions, there were eleven deaths, which were due to the gastrointestinal lesions and not to the oral malignancies.

CASE REPORTS

Two illustrative case histories are presented, one involving a 71-year-old man (Patient 8, Table I) and the other involving a 39-year-old woman (Patient 1, Table I).

Case 1.—A 71-year-old married white man was admitted to the Westfield State Sanatorium on Nov. 25, 1953, with a diagnosis of multiple carcinomas of the oral cavity. Three months prior to admission he had first noticed a growth on the lateral margin of the left side of the tongue. The lesion had grown rapidly but had always been painless and free of bleeding. He stated that for six months he had had a chronic toothache adjacent to this lesion and that recently the tooth had been extracted with relief of pain. A biopsy of the tongue lesion at that time revealed it to be an epidermoid carcinoma. There had been no loss of weight.

A review of systems and of the past history was essentially negative. The patient had been a very heavy pipe smoker for approximately forty years.

Physical examination revealed a fairly well-developed and well-nourished elderly white man in good health. The positive physical findings were limited to the mouth. Examination of the oral cavity revealed five primary carcinomas of the mouth, as follows:

(1) A 3.5 cm. exophytic lesion of the posterior two-thirds of the lateral border of the tongue on the left (Fig. 1).
(2) An ulcerated 2.5 cm. exophytic lesion of the left anterior floor of the mouth (Fig. 3).
(3) A 1.5 cm. indurated exophytic growth situated on the posterior third of the right lateral margin of the tongue (Fig. 2).
(4) A 1.5 cm. indurated, elevated white plaque of the left buccal mucosa (Fig. 1).
(5) A 2.0 cm. elevated, hard, white lesion of the right buccal mucosa (Fig. 2).

All five lesions were biopsied and proved to be malignant. Examination of the neck revealed several readily palpable hard lymph nodes situated along the anterior margin of the left sternocleidomastoid muscle; there were no other palpable cervical lymph nodes.

On Dec. 1, 1953, the patient had all his remaining teeth removed prior to the start of radiation therapy. During his hospitalization he received intensive intraoral irradiation to all lesions; this was supplemented with external radiation. During the course of treatment there was a rather marked enlargement of the left cervical lymph nodes, particularly in the left supraclavicular area along the anterior margin of the sternocleidomastoid muscle. These nodes reached the size of 2.5 cm. in diameter and were firm; the entire area was matted and indurated. As a result of the x-ray therapy, there was marked improvement in the appearance of the oral lesions. By Feb. 11, 1954, the left posterior tongue tumor was approximately one-third its original size, and, because of its minimal size, the right posterior lingual lesion could be visualized only with difficulty. Both buccal mucosal lesions were virtually gone. In addition, there was an extensive mucositis of the entire mouth. Biopsies of all five lesions done prior to the patient's discharge from the hospital on February 11 were reported as follows: "All lesions showed leukoplakia with one lesion showing evidence of one or two mitotic figures." The prognosis was considered hopeless. The patient died on Feb. 24, 1954, and an autopsy was not performed.

Case 2.—A 39-year-old married white woman was first seen on Feb. 18, 1955, because of bilateral 1.5 cm. exophytic, painful growths in the premolar-molar regions. These had previously been excised in March, 1954, and had been diagnosed as benign papillomas; radiographs taken at that time were also negative. These growths had recurred in January, 1955. The past history was essentially noncontributory except for very heavy smoking.

On Feb. 21, 1955, these lesions were widely excised and were reported as papillomas with surrounding chronic inflammation. The teeth were scaled and the occlusion was adjusted so as to eliminate the possibility of traumatic occlusion. By April 21, 1955, both lesions had started to recur and the right area had undergone slight ulceration. On June 20,

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1.—Exophytic lesion of the left lateral border of the tongue and indurated plaque on the left buccal mucosa in a 71-year-old man.

Fig. 2.—Raised lesion on the right lateral border of the tongue and elevated white plaque on the right buccal mucosa in a 71-year-old man.

Fig. 3.—Raised verrucous lesion on the floor of the mouth in a 71-year-old man.

1955, both areas were again totally removed as excision biopsies, since the right and left areas had markedly enlarged (Figs. 4 and 5). The right side had developed a large ulceration which bled freely on palpation. Both biopsies were reported as epidermoid carcinoma. The patient elected to go to a nearby clinic where, on June 28, 1955, the lower teeth were extracted, the overlying gingivae with a 1.0 cm. buccal and lingual margin were excised, an extensive alveolectomy was done, and a lymph node attached to the left facial vein where it crossed the mandible was removed. No residual tumor was found on pathologic examination and the lymph node was negative for metastatic carcinoma. The patient remained free of recurrent or new carcinoma. She did not smoke after the surgical procedure of June 28, 1955.

Fig. 4.

Fig. 5.

Fig. 4.—Leukoplakia and early carcinoma of the right gingiva in the cuspid-premolar area in a 39-year-old woman.

Fig. 5.—Verrucous carcinoma with central area of ulceration on the left gingiva in the premolar area in a 39-year-old woman.

On July 5, 1957, the patient returned with an area of extensive clinical leukoplakia involving the major portion of the ventral surface of the tongue. Because of her past history, she was advised to have the area biopsied and either excised or electrodesiccated. However, the patient elected to return to the clinic where the surgery had been performed. There she was advised that frequent observation of the area would suffice, and this is the course which she is presently following.

DISCUSSION

This study corroborates previous observations that a patient with one carcinoma of the mouth has an increased chance of developing a second malignancy of the oral mucosa. Our observations further indicate that there is also a tendency for persons with oral malignancies to develop malignant tumors elsewhere in the gastrointestinal tract.

We feel that multiple malignancies of the oral mucosa and the gastrointestinal tract are not incidental occurrences, a viewpoint expressed by Hanlon,[17] but are a similar, organized response to some influence acting throughout the mucosa. Lund[19] has demonstrated that the occurrence of oral multiple malignancies was approximately fifteen times as common as would be expected

by chance occurrence alone. Our findings of multiple oral primary carcinomas, using Greenberg's method of analysis,[28] are eight times that of chance occurrence; this is statistically very significant ($X^2 = 196.8$ for one degree of freedom).

Statistically, no excess cases of cancer of the gastrointestinal tract were observed. According to rates established for the state of Connecticut, 15.699 cases could have been expected; our findings of eighteen cases were not statistically significant. Despite our inability to demonstrate statistical significance of the relationship of oral primaries and gastrointestinal primaries, we feel that clinically there is a definite relationship. Greenberg[28] found a significant increase in the number of cases of second primaries of the gastrointestinal tract following a first primary of the oral cavity.

We have followed general criteria laid down for a consideration of multiple malignancies. The gross and microscopic appearances of the multiple oral lesion were similar to those usually seen in individual malignant tumors of the oral mucosa. In all cases the lesions were separated by a large area of clinically normal tissue. In order to remove any doubt, we considered only lesions that were distant from one another and only lesions on opposite sides of the tongue, lip, and gingiva. In many cases we were able to confirm by microscopic study that the margins of the lesion consisted of normal tissue. In some cases the margins of the carcinoma presented evidence of leukoplakia or carcinoma in situ, indicating a transitional zone from normal to neoplastic tissue. We could not utilize the criteria of Goetze[26] in relation to similarity of metastasis to the original multiple lesions. In only seven of our cases was there any evidence of metastatic spread from the primary oral lesions. This relative absence of metastasis lends further support to the consideration of these multiple lesions as primary tumors rather than as metastases spread from one site to another.

We did not find adequate correlation between development of multiple oral cancer and smoking or syphilis. This correlation has been reported by Sarasin[10] and others.[14, 24]

CONCLUSIONS

1. There is an increased tendency for a person with one oral malignancy to develop another malignant tumor of the oral mucosa. There is a lesser tendency for these patients to develop malignancies elsewhere in the gastrointestinal tract.

2. Cases of oral malignancy should be carefully and systematically followed at regular, frequent time intervals with a view to the tendency for development of additional lesions.

3. The occurrence of premalignant lesions or lesions noted as precursors of malignancy, such as leukoplakia, should be aggressively dealt with in patients who have a history of previous oral carcinoma.

4. Careful evaluation and removal of all local irritation in a mouth with a previous history of carcinoma are essential. This irritation would include

defective dentures and restorations, sharp, malposed teeth, etc. Existent infection, either periapical or periodontal, should also be eliminated. Until we have further definite information, we must accept continual chronic irritation of the mucosa in susceptible persons as an etiological factor of prime importance in the development of malignancy.

5. Gastrointestinal symptoms in patients with previous oral carcinoma must be carefully evaluated by the internist or gastroenterologist.

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THE FATE OF THE HUMAN FOLLICULAR SAC IN HETEROLOGOUS TRANSPLANTATION

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THE stimulating influence for this experimental study of the fate of odontogenic epithelium in the dental follicle was the result of the many references in the literature indicting odontogenic and oral epithelium in the development of the ameloblastoma.[1-9] These references, however, were theoretical and not experimental.

The dental follicle, or follicular sac, is a fibrous connective tissue wall which varies from a loose, fibrillar stroma to a mature type with abundant collagen and surrounds the tooth during embryological development. Early in embryonic development the inner margin of the follicular sac is in intimate contact with the outer enamel layer of cells. Later, when the crown is fully formed and assumes its functional position, the follicular sac condenses and becomes part of the supporting connective structure at the coronal portion of the tooth (Fig. 1).

In the case of the impacted or embedded tooth, the condensed follicular sac persists and surrounds the coronal portion of the tooth, occupying a cryptic space within bone (Fig. 2). The reduced enamel epithelium now lines the inner margin of the follicular sac adjacent to the enamel. Portions of this odontogenic epithelial structure may persist as lining epithelium, or as clusters, cords, or nests of epithelial cells in the connective tissue stroma of the follicular sac (Figs. 3 and 4).

In our findings, which substantially supported the findings of Jacobs,[10] Gettinger,[11] and Conklin and Stafne,[12] histopathologic studies of 200 individual human follicular sacs from impacted teeth revealed the presence of epithelium, in the form of lining or cell rests, in approximately 80 per cent of the cases (Figs. 3 and 4).

It is these odontogenic epithelial cell elements, the lining, cords, or rests of the follicular sac, which have been designated as the progenitors of odontogenic cysts and tumors.

By heterologous transplantation of human follicular sacs associated with embedded or impacted teeth, we attempted to trace the pathogenesis of these

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epithelial and connective tissue elements of the follicular sac to the development of odontogenic cysts and tumors, principally the ameloblastoma.

EXPERIMENTAL PROCEDURE

A group of twenty-five young adult stock guinea pigs, weighing approximately 500 grams each, were used as the recipients for the implantation of

Fig. 1.

Fig. 2.

Fig. 1.—Photomicrograph of developing tooth showing follicular sac *(A)* and dentine *(B)*. (Magnification, ×75; reduced ⅓.)

Fig. 2.—Roentgenogram of impacted tooth with bone crypt outlining follicular sac.

human follicular sacs. The follicular sacs, removed from embedded or impacted teeth in patients varying in age from 8 to 50 years, were immediately placed in sterile, refrigerated Ringer's solution following surgery, and sections

Fig. 3.

Fig. 4.

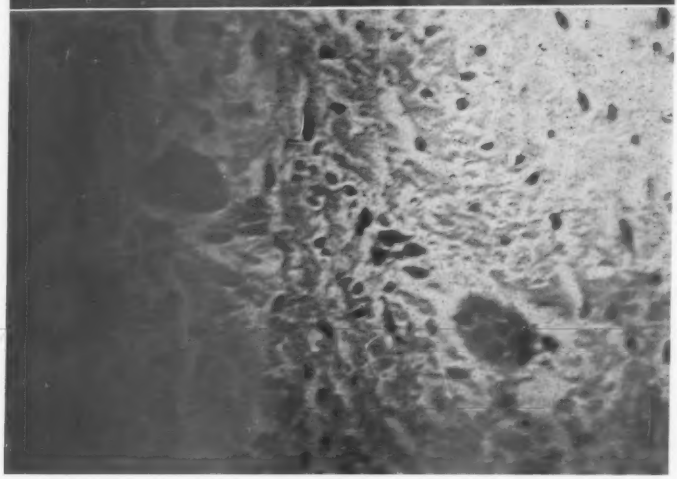

Fig. 3.—Photomicrograph of follicular sac showing epithelial lining. (Magnification, ×250; reduced ⅝.)

Fig. 4.—Photomicrograph of follicular sac showing epithelial islets in connective tissue matrix. (Magnification, ×250; reduced ⅝.)

of the sac were transplanted within an hour into the anterior chamber of the eye of the guinea pig. The method of transplantation was essentially the same as that employed by Fleming.[13-15] The remainder of the sac was placed in 10 per cent formalin and prepared for microscopic analysis. The animals were

observed daily for evidence of changes in the implant relative to growth. The animals were then sacrificed by intraperitoneal injection of pentobarbital sodium at varying intervals from 62 to 216 days after the initial transplantation of the human follicular implant.

The eyes were removed and placed in 10 per cent formalin for fixation in preparation for serial hematoxylin and eosin paraffin sections. Decalcification was employed where considered necessary.

OBSERVATIONS

Gross.—The initial changes in the eye in the first and second weeks following transplantation revealed grossly an inflammatory process with edema. Following this period, the inflammatory response resolved itself and the cornea, sclera, and anterior chamber were clear, disclosing the implant in its position in the anterior chamber at the corneal-iris angle.

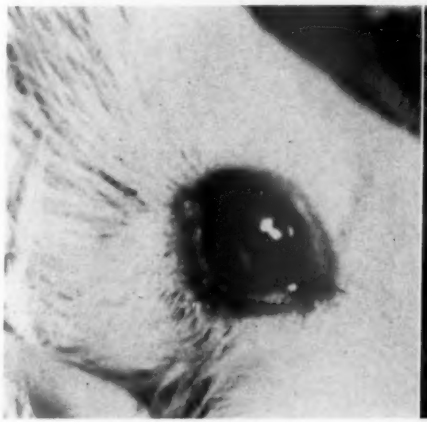

Fig. 5.

Fig. 6.

Fig. 5.—Photograph of guinea pig's eye showing transplant in anterior chamber twelve days postoperatively.

Fig. 6.—Photograph of guinea pig's eye showing transplant in anterior chamber 109 days postoperatively.

In general, definite growth of the implant was observed at the end of 30 days, with a bluish gray halo surrounding the mass. Slight bulging of the anterior chamber was also noted at this time and was attributed to the accumulation of fluid.

As time progressed, up to 216 days, the transplanted mass increased in size and showed a change in color from gray-white to pink-brown, with the bluish gray halo persisting (Figs. 5 and 6).

Microscopic Analysis of Transplanted Follicular Sac.—

The follicular sac at the time of transplantation: Sections revealed a fibrous connective tissue stroma which varied from a loose, fibrillar type to a more dense, collagenous one. Scattered throughout this stroma were isolated

Fig. 7.

Fig. 8.

Fig. 7.—Photomicrograph of follicular tissue transplanted into anterior chamber showing lining epithelium. (Magnification, ×250; reduced ⅝.)

Fig. 8.—Photomicrograph of follicular tissue transplanted into anterior chamber showing clusters of epithelial cells. (Magnification, ×250; reduced ⅝.)

nests, strands, and clusters of epithelial cells. When epithelium was present at the surface, a low type of stratified squamous epithelium was seen. Foci of inflammatory infiltrations were meager or absent (Figs. 7 and 8).

Fate of the transplanted follicular sac: The predominant microscopic features found in the majority (70 per cent) of the experimental animals revealed the following:

(a) At the end of 62 days the implanted follicular tissue in the anterior chamber disclosed a proliferating connective tissue mass

Fig. 9.

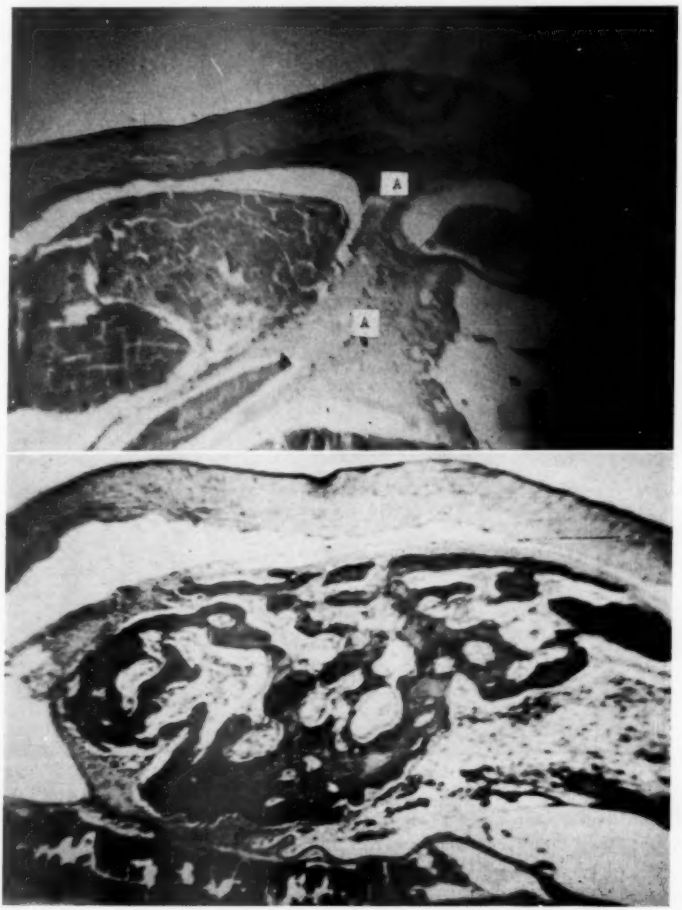

Fig. 10.

Fig. 9.—Photomicrograph of proliferating connective tissue of the transplant *(A)* within the anterior chamber of the eye at the end of sixty-two days. (Magnification, ×250; reduced ⅝.)

Fig. 10.—Photomicrograph of proliferating connective tissue of transplant with differentiation into osteoid and osseous lamellae after 119 days. (Magnification, ×250; reduced ⅝.)

which consisted of numerous fibroblasts trapped in a collagenous matrix. There was evidence of hyalin degeneration throughout the sections (Fig. 9).

Fig. 11.

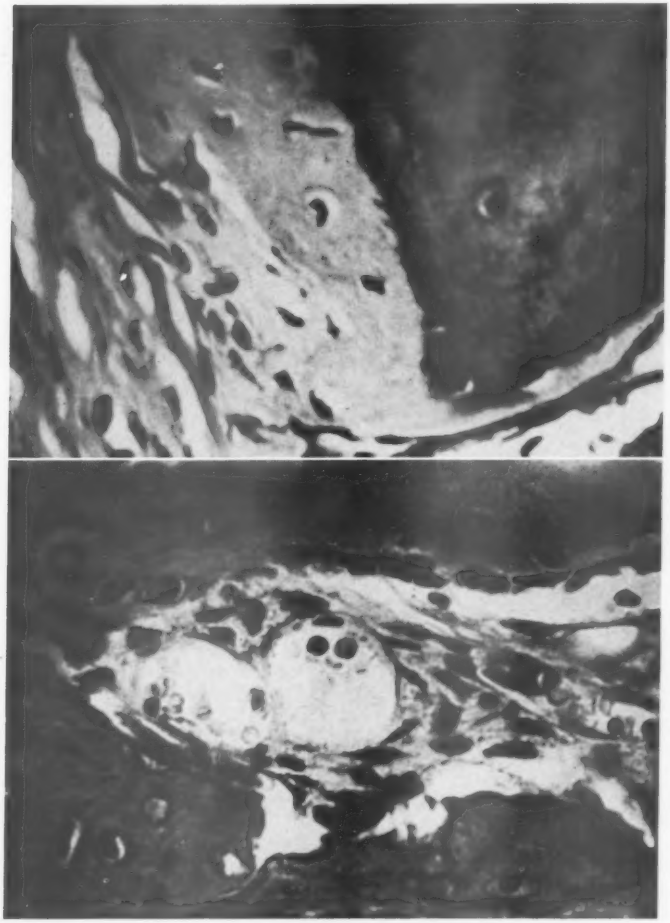

Fig. 12.

Fig. 11.—Photomicrograph showing osteoid seams surrounding foci of mature bone. Osteoblasts are lining the osteoid tissue. (Magnification, ×600; reduced ⅝.)

Fig. 12.—Photomicrograph showing a vascular, loose connective tissue stroma in the marrow space. (Magnification, ×600; reduced ⅝.)

(b) During the period between 119 and 216 days after the transplantation, within the anterior chamber at the corneal-iris junction, seams and trabeculae of osteoid and bone were deposited in a substratum of vascular, osteogenic connective tissue (Fig. 10).

(c) The bone tissue was viable and contained normal osteocytes in their respective lacunae (Fig. 11).

(d) In many cases the marrow within the bone trabeculae revealed a highly vascularized, loose connective tissue stroma (Fig. 12).

(e) In some cases cellular elements of hematopoietic tissue were enmeshed within the marrow stroma (Fig. 13).

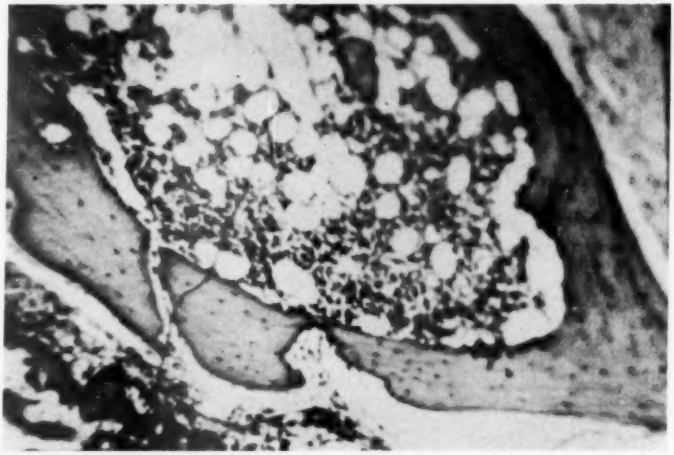

Fig. 13.—Photomicrograph showing the marrow space filled with hematopoietic tissue. (Magnification, ×250; reduced ⅝.)

(f) Osteoblasts lined the periphery of the osteoid seams. These cells appeared to be derived from the connective tissue of the transplanted follicular sac (Fig. 11).

(g) In a few sections, we observed calcified material which gave the impression of being cementum-like in character (Figs. 14 and 15).

(h) The vascularity and vitality of the transplanted tissues were maintained by vascular channels extending from the iris into the implant (Fig. 16).

(i) In relatively few instances (six), no evidence of transplant could be observed grossly or microscopically (Fig. 17).

DISCUSSION

Greene[16-19] and Fleming,[13-15] in their experiments with heterologous transplantation of embryonic and malignant tissues, have shown the ability of these cellular elements to survive, differentiate, and proliferate. If the epithelial elements of the follicular sac possessed embryonic capacity for growth, it would have been observed in our experimental results. Since this capacity for growth was not evident in our experimental findings, it is reasonable to assume that these epithelial cells apparently lacked the embryonic or neoplastic capacity

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for growth, or that this capacity for growth, although inherently present, may have been interfered with or altered by (1) an unknown factor of the local environment present in human beings which may be different in the experi-

Fig. 14.

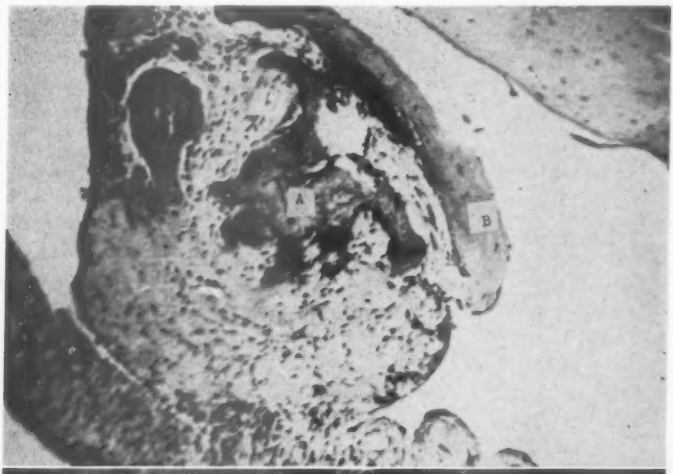

Fig. 15.

Fig. 14.—Photomicrograph of transplant showing calcified tissue which gives the impression of being cementum *(A)*. A laminar spicule of bone can also be seen *(B)*. (Magnification, ×250; reduced ⅝.)

Fig. 15.—High-power view of section shown in Fig. 14 showing cementum-like structure. (Magnification, ×600; reduced ⅝.)

mental animal, (2) overwhelming influence of the connective tissue elements which suppress the proliferative ability of the epithelial cells in the implant, or (3) technique and conditions employed in this experiment.

Our experimental findings reveal that the connective tissue elements of the transplanted follicular sac were able to survive, proliferate, and differentiate into collagen, bone, and cementum-like structures. These findings sub-

Fig. 16.

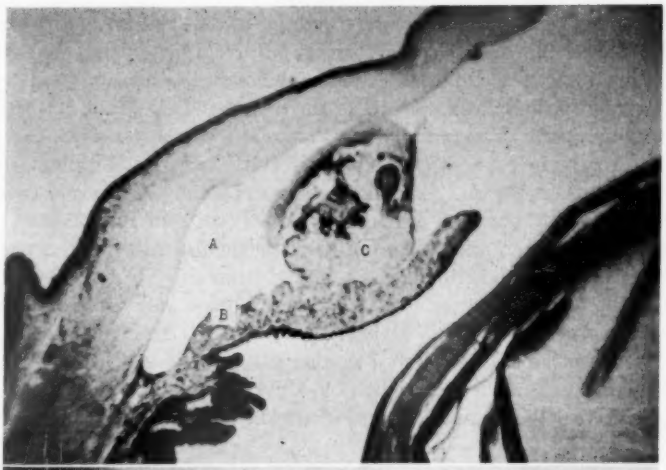

Fig. 17.

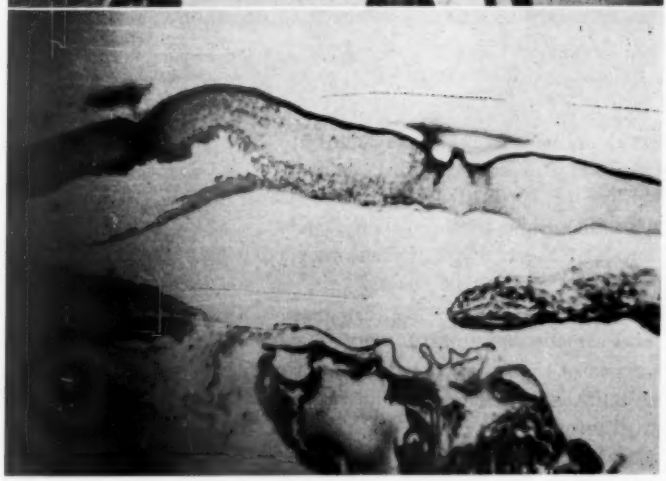

Fig. 16.—Photomicrograph of anterior chamber *(A)* showing vascular channels of the iris *(B)* nourishing the transplant *(C)*. (Magnification, ×75; reduced ⅝.)

Fig. 17.—Photomicrograph of anterior chamber without evidence of the transplant. (Magnification, ×75; reduced ⅝.)

stantiate the inherent ability of the connective tissue components of the dental follicle to differentiate and mature into bone and cementum-like structures. It is possible that the epithelium present in the dental follicle as either surface

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lining, cords, clusters, or nests of cells was the early inducting influence on the connective tissue elements, stimulating them to differentiate and mature into bone and cementum. Theoretically, this concept supports the findings of other investigators who have reported on the influence of epithelium in the development of heterotopic or ectopic bone formation.[20-25]

On the basis of our experimental findings of the ability of the connective tissue elements of the dental follicle surrounding impacted or embedded teeth to survive, proliferate, and differentiate into bone and cementum-like structures, and whereas the epithelial components of the dental follicle could not be observed in any of our sections, it is reasonable to assume that these results can offer an explanation for the infrequent clinical manifestation of ameloblastoma in human beings. Thus, when partially or completely impacted teeth are removed and the dental follicle or portions of it inadvertently remain in the jaws, there is only a remote possibility that these epithelial elements may survive, proliferate, and differentiate into odontogenic cysts and tumors. The connective tissue elements of the follicle, however, will mature into bone and become a part of the normal repair process. Since in certain isolated cases there exists the possibility of the presence of unknown factors in the jaws which may stimulate the epithelial elements of the dental follicle to develop into odontogenic cysts and tumors, we advise the complete excision of the dental follicle at the time of surgery.

We are currently conducting research to determine the fate of the epithelium in the dental follicle.

SUMMARY

1. Dental follicles were removed from impacted or embedded teeth of human beings varying in age from 8 to 50 years.

2. Portions of these dental follicles were transplanted to the anterior chamber of guinea pigs' eyes.

3. Growth of the transplant was observed within the anterior chamber of the eyes in 70 per cent of the cases.

4. Microscopic analysis of the transplanted tissue revealed growth of bone, collagen, and cementum-like structures.

5. In six cases there was no evidence of survival or growth of the transplant.

6. The epithelial elements of the transplanted tissue did not survive, proliferate, or differentiate in any of the cases.

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INFANTILE HEMANGIOENDOTHELIOMA OF THE TONGUE

Irwin A. Small, D.D.S., and Gilbert S. Small, D.D.S., Detroit, Mich.

THE hemangioendothelioma is an uncommon tumor, and until recently its place in the classification of blood vessel tumors met with little unanimity of opinion. There has been a paucity of descriptions of this tumor in the dental literature, and statistical studies are infrequent in the medical literature. By September, 1951, Stout[1] had recorded a total of only thirty-four patients with malignant hemangioendothelioma. Cheyne and Silberstein[2] have reviewed the literature and mention the tumor's rare occurrence in the oral cavity. The infantile or benign form of this tumor occurs more frequently than the malignant hemangioendothelioma, and it is seen most commonly in the skin and subcutaneous tissues. A case will be presented and the relationship of the infantile form to the hemangioendothelioma will be discussed.

Golgi[3] introduced the term endothelioma in 1869 but did apply it specifically to vascular tumors. The hemangioendothelioma was described by Borrmann[4] in 1899. Mallory[5] used this term in 1908 to describe a malignant vascular tumor and pointed out that the endothelial cell is responsible for the aggressive growth and metastatic potential of this tumor. Ewing[6] preferred the general term endothelioma, which described a variety of vascular tumor, the cell type of which was morphologically similar to the endothelial cell of blood and lymph vessels. He described the hemangioendothelioma as occurring chiefly in the skin and subcutaneous tissues of children, exhibiting a slow growth pattern, and consisting of a diffuse growth of endothelial cells with imperfect formation of capillaries. Willis[7] preferred not to classify angiomatoid tumors according to specific vascular origin but to group them as variants of the genus mesenchymoma. Others divide vascular tumors into benign angiomas and angiosarcoma.[8, 9] Stout's[10] article in 1943 clarified the histopathology of this tumor. Stout's criteria have been the basis for identification of this tumor and its relationship to other vascular tumors. He maintains there are three vascular tumors characterized by the formation of vascular tubes which may have malignant potential. These are derived from the normal components of blood vessels. The hemangiopericytoma is derived from the pericyte, the contractile element of capillaries. This tumor is usually benign, although a malignant variety has been reported. It is found commonly in the soft tissues. Its best known varient is the glomus tumor, most commonly found beneath fingernails. The second type is formed from the

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smooth muscle component of blood vessels, the leiomyoma. These are most commonly subcutaneous tumors. Although a leiomyosarcoma derived from blood vessels may be possible, it is extremely difficult to establish vascular origin. The third group, which stems from the endothelial cell, is the hemangioendothelioma. This tumor, as it occurs in the adult, may arise in any tissue and is considered to be a malignant neoplasm, capable of early and widespread metastasis.[1, 10] The tumor appears to have a benign counterpart which occurs mainly in infants; it most commonly involves the skin and frequently involves liver and parotid gland. It is with this tumor that we are mainly concerned.

CASE REPORT

A 3-day-old white boy was seen with a 0.5 cm. slightly raised, round mass on the left mid-dorsum of the tongue (Fig 1). The lesion was bluish red, soft to palpation, and exhibited slight blanching on pressure. The clinical impression was congenital hemangioma.

Fig. 1.—Bluish red mass, 0.5 cm. in diameter, on the tongue of a 3-day-old infant.

There were diffuse areas of capillary hemangioma in the skin of the occipital and frontal regions. It was felt that the tumor should be observed for a period of a few months to see if any regression might occur. Slow growth was observed for four months. In the fifth month a sudden increase in size was noted, and spontaneous bleeding occurred. Bottle feeding became difficult, and the patient was admitted to the hospital (Fig. 2). Examination revealed a tumor mass, 2.5 cm. in diameter, round, and markedly raised. There was ulceration of the overlying mucosa. The tumor was soft to palpation, did not blanch, and did not appear fixed to the underlying tissues. Several small cervical nodes were palpable. The diffuse capillary hemangiomas of the skin were unchanged. The remainder of the physical examination revealed a normal male infant. There was no family history

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of bleeding or similar involvement. The patient was typed and cross-matched for blood. On the following day, under endotracheal anesthesia, a cut-down was done to secure a vein for necessary blood replacement. A small segment of tumor was removed for frozen section and was reported to be a cellular hemangioma. The tumor was removed by sharp dissection with minimal margins of normal tissue. Blood loss was estimated at 50 ml. and was immediately replaced. The postoperative course was uneventful.

Fig. 2.—At 5 months of age, growth and ulceration of the tumor mass had occurred.

Pathologic Findings.—The report of the surgical specimen was as follows:

Gross pathology: The specimen consisted of a rounded piece of firm, gray-pink-tan tissue which measured 2.3 by 1.8 cm. One area was covered by a glistening white epithelium, in the central portion of which was a raised, round, firm variegated tumor which comprised most of the specimen.

Histopathology: Microscopic examination showed a fragment of tongue which included, to either side, stratified squamous epithelium with prominent rete pegs, well-glycogenated with areas of cornification and aggregations of bacterial colonies in the clefts of the surface in a characteristic manner (Fig. 3). A central elevation had been formed by granulation tissue replacing the epithelium abruptly and overlying a tumor mass which had infiltrated and replaced underlying muscle (Fig. 4). The surrounding submucosal connective tissue was somewhat thickened and blended into the neoplastic mass. At the surface there were vessels of capillary caliber, heavily infiltrated with polymorphonuclear leukocytes, histiocytes, and scattered plasma cells with condensation of fibrous tissue in the characteristic manner of granulation tissue. There were abrupt large dilations of lumina of capillary channels forming cavernous places lined by well-differentiated flattened endothelium (Fig. 5). These cavernous spaces were more infrequent but in themselves larger in the depths, where there was a transition to a more solid and cellular tumor formed by fusiform cells with relatively large, elongated, vesicular nuclei with chromatin condensation in places but without true nucleoli in most instances (Fig. 6). There was minimal nuclear pleomorphism but no mitotic activity. There was persistent infiltration by inflammatory cells into the depths, but in reduced numbers. Most often the vascular spaces were potential rather than real. They occurred erratically and were lined by elongated cells, with fibrillar cytoplasm forming the mass of the tumor. There was some fasiculation and whorling, but in general there was little polarity of tumor cells in relation to one another.

Muscle fibers were incorporated and were preserved to a variable degree (Fig. 7). In the depths the advancing tumor was preceded by condensation of connective tissue in

Fig. 3.

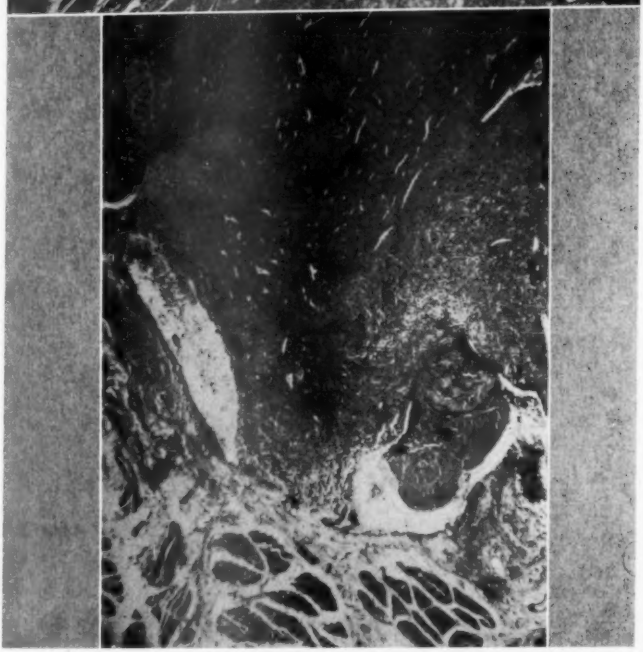

Fig. 4.

Fig. 3.—The superficial portion of the tumor showing ulceration and granulation tissue with anastomosing vascular channels noted in the depths. (Magnification, ×25; reduced ⅛.)

Fig. 4.—The base of the lesion showing feeding vessels, lack of encapsulation, and invasion of muscle. The majority of the tumor is cellular with formation of small anastomosing channels. (Magnification, ×25; reduced ⅛.)

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which were imprisoned muscle fibers in states of resorption, with occasional larger fibers with hyperchromatic nuclei representing degenerating fibers. The inferior and lateral limits of the resection were clear of tumor. Reticulin stains (Fig. 8) demonstrated continuity of reticulin from about vascular spaces into the more solid portion of the tumor, suggesting

Fig. 5.

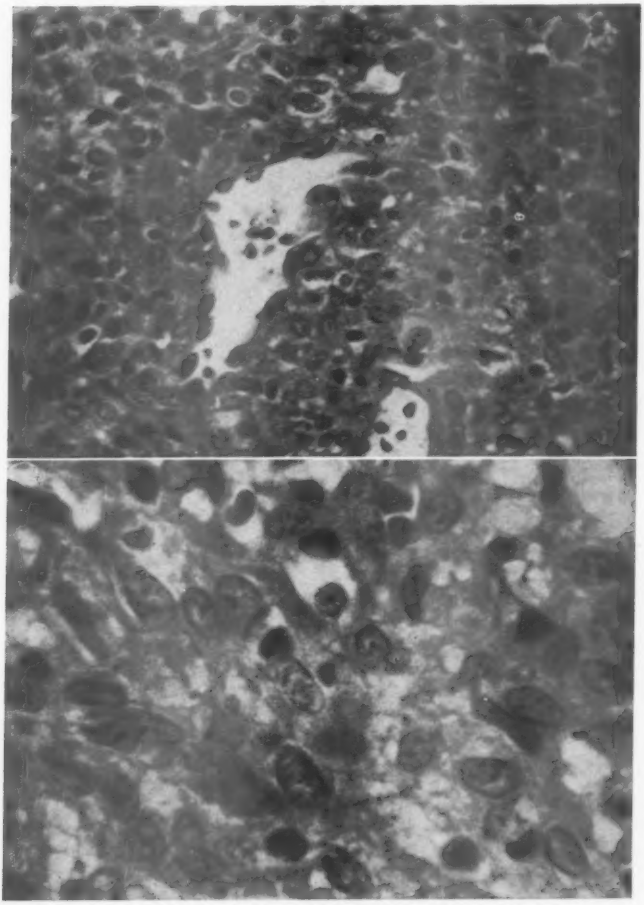

Fig. 6.

Fig. 5.—Section showing a well-formed vascular channel lined by plump, mature, endothelial cells. The majority of the tumor is cellular with some suggestion of variation of nuclear size and shape. (Magnification, ×300; reduced ⅛.)

Fig. 6.—Section showing cellular detail, the elongated vesicular nuclei, and fibrillar cytoplasm. Although this portion of the tumor is very cellular, vascular spaces are being formed, some filled with blood cells. (Magnification, ×600; reduced ⅛.)

that the cells lining the vascular spaces (which were, incidentally, filled with blood) were histogenetically and morphologically identical to those forming the solid portions of the tumor.

Anatomic diagnosis:* Juvenile, cellular hemangioendothelioma of the tongue.

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*Saul Brown, M.D., Pathology Department, Sinai Hospital.

DISCUSSION

Stout[10] points out the two features of hemangioendothelioma which are uniformly present in these tumors: "First, the formation of atypical endo-

Fig. 7.

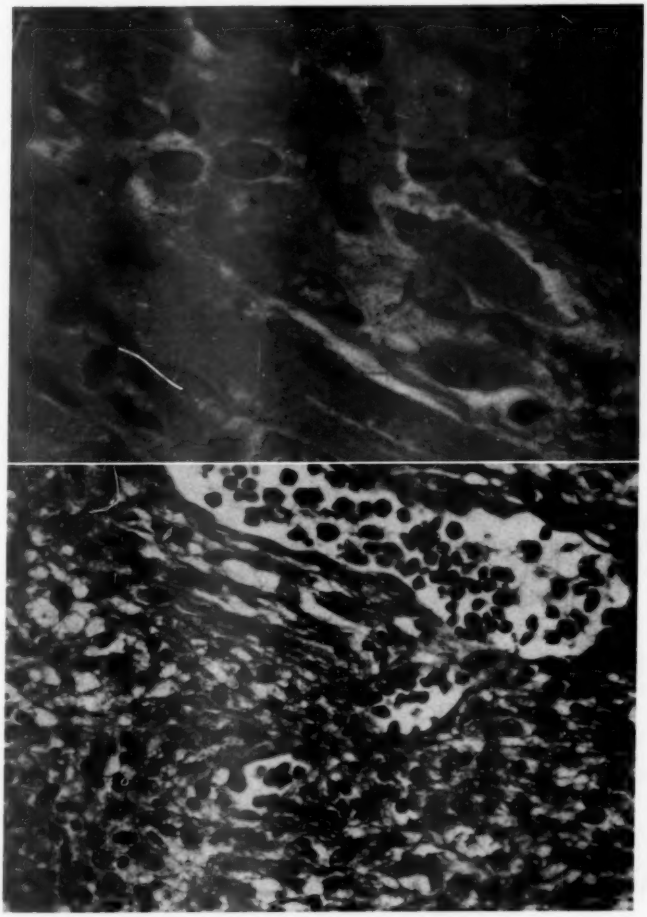

Fig. 8.

Fig. 7.—Section showing invasion of muscle and the pyknotic, elongated, swollen nuclei of muscle fibers. A mitotic figure can be seen at the midportion of the field. (Magnification, ×600; reduced ⅛.)

Fig. 8.—Section showing the reticulin fibers about the well-formed capillary channels and also about the cells in the solid portion of the tumor, establishing these cells as endothelial rather than perithelial. (Silver reticulin stain. Magnification, ×300; reduced ⅛.)

thelial cells in greater numbers than are required to line the vessels with a simple endothelial membrane, and the second, the formation of vascular tubes with a delicate framework of reticulin and a marked tendency for their

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lumens of anastomose. No tumor should be considered a hemangioendothelioma unless these criteria are both present." In addition, there may be variations in size, shape, number, and staining characteristics of endothelial cells that serve to emphasize the malignant quality of the neoplasm. The cellular elements may form a single layer or may pile up and fill the vascular tubes. They may penetrate these tubes and grow in solid sheets.[1] These features serve to differentiate this tumor from the benign angioma and the benign hemangioendothelioma. Special stains for reticulin may be utilized to show the relationship of these cells to the reticular framework. A silver reticulin stain will locate the proliferating cells of the hemangioendothelioma within this framework, while the cells of the hemangiopericytoma will be outside.

The tumor that has been presented appears to uphold the criteria for a hemangioendothelioma. Growth, although rapid, appears orderly under the microscope. Although the tumor is not encapsulated and appears to be infiltrating, there is no evidence of any real variation in size, shape, and staining characteristics of the endothelial cells. The location of this tumor and the constant irritation during feeding periods may have stimulated growth. Stout[11] points out, however, that a malignant form of hemangioendothelioma can develop in children as well as in adults but that the morphology of this should be easily distinguished from the benign, infantile form.

There is one variant of the infantile hemangioendothelioma which has caused much confusion. We refer to the variety that has multiple lesions not only in the superficial tissues but in the viscera as well. These can cause death because of the multiplicity of areas of involvement. There have been increasingly frequent reports of such tumors involving the liver in children.[11-14] In the cases with extensive liver involvement, the presenting symptoms may be those of cyanosis and dyspnea associated with cardiomegaly and hepatomegaly. The suggested diagnosis is congenital heart disease with decompensation, and the presence of the liver tumor may not be suspected. It has been demonstrated that the cardiovascular signs have resulted from the hemodynamic effects of this highly vascular tumor. The infantile hemangioendothelioma appears capable of producing an arteriovenous shunt of sufficient magnitude to produce death by congestive failure. In other instances of liver involvement death was due to hepatic failure.[12]

Anderson,[15] writing on tumors of infancy and childhood, offers an interesting hypothesis concerning the evolution of hemangioendothelioma in young children. She maintains that the cellular hemangioendothelioma represents a less mature stage in the development of a hemangioma. To support this hypothesis, the slides from sixty-five consecutive cases of hemangioma were examined, the age of the patients being unknown at the time. They were graded in four categories: Those in which more than one-half of the tumor was composed of solid cells, those in which one-fourth to one-half of the tumor was solid, capillary hemangioma, and cavernous hemangioma. When the ages of the patients were correlated with the specimens, it was noted that thirty, or about 80 per cent, of the solid tumors occurred in children

up to 2 years of age and the majority of the tumors occurring between the ages of 12 and 14 were capillary and cavernous hemangiomas. It was concluded that the hemangioendothelioma of infants may be expected to mature into the capillary type of hemangioma, enlarging in the process up to the age of about 2 years but not becoming malignant.

The impression that the hemangioendothelioma in infants resembles the common hemangioma of the skin is supported by others.[13] Like the latter lesion, it may have a natural history of rapid growth followed by spontaneous regression. There may be morbidity and mortality in some cases with multiple areas of involvement or with extensive visceral involvement. In a case such as the one presented here, in which there is a solitary oral lesion, the possibility of multiple foci should be ruled out. Although there were a few diffuse capillary angiomas of the skin, no other areas of tumor involvement were noted in our case. Treatment should be conservative, as in the case of hemangioma, after the establishment of a diagnosis. If excision is indicated, the possibility of severe blood loss should be anticipated.

SUMMARY

A case of infantile hemangioendothelioma of the tongue has been presented. Although the microscopic picture is that of a highly cellular, unencapsulated, infiltrating tumor and the clinical picture is one of rapid growth, these appear to be benign tumors. They tend to occur most frequently from birth to the age of 2 years, and spontaneous regression may be expected to occur. The variety of lesion that has multiple foci may produce death because of extensive involvement of vital areas. The presence of angiomas of the skin with a rapidly growing tumor of the liver or other organs should suggest the possibility of infantile hemangioendothelioma. After diagnosis has been established, treatment should be conservative and will depend upon the location of the tumor.

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7411 Third St.

SYMPOSIUM ON PULP REACTION TO OPERATIVE PROCEDURES

Harold Stanley, D.D.S., M.S., B.S., Bethesda, Md., Helmut Zander, M.S., D.D.S., Rochester, N. Y., H. B. G. Robinson, D.D.S., M.S., Kansas City, Mo., and Joseph L. Bernier, Colonel, USA (Moderator)

DR. STANLEY'S presentation is a report of investigation carried out by Dr. Herbert Swerdlow and himself. The summary follows:

The purpose of this study was to determine which operative techniques involving a combination of speed, cutting tool, coolant, and load permitted cavity preparation with minimal pulpal reaction. The speeds ranged from 6,000 r.p.m. to over 200,000 r.p.m. The cutting instruments consisted of inverted-cone No. 37 diamond stones, No. 36 diamond stones, and No. 35 carbide burs. The coolants accompanying the procedures were air-water spray, water, or air. Loads varied from 1 to 10 ounces with the higher speeds to 8 to 24 ounces with the low speeds.

Class V cavity preparations were cut on the facial surfaces of more than 450 intact human teeth and filled with zinc-oxide and eugenol. The specimens were extracted at intervals of less than one hour to 132 days. Comparisons were made between the different techniques by recording the incidence and intensity of specific histopathologic characteristics.

Speeds at 50,000 r.p.m. and over, both of the belt-driven or turbine type cutting with the No. 36 diamond stone and the No. 35 carbide bur, were found to be less traumatic to the human pulp than the 6,000 and 20,000 r.p.m. techniques using the conventional ball-bearing handpiece and the No. 37 diamond stone and the No. 35 carbide bur. The value of coolants becomes more significant at the higher speeds. Preparation time at the higher speeds is of little consequence, provided frictional heat is controlled by adequate coolants. The combination of high speed, controlled temperature, and minimum load is conducive to minimal pulpal pathology.

Cutting efficiency is so greatly improved with the increased speed that the clinician is given the opportunity to decrease the potential trauma of cavity preparation by using smaller cutting instruments which give increased biologic safety at any speed. Excessive temperature rise was apparently controlled by air-water sprays and water at all speeds except 6,000 r.p.m. when used in combination with a No. 37 diamond stone and a load of 16 to 24 ounces.

Dr. Zander summarizes his presentation briefly as follows:

The dental pulp is capable of certain reactions to injury from dental instruments, such as displacement of cells, inflammation, and its sequelae. Regardless of speed, operative techniques may produce pulp injury. However, extra precautions must be taken when using high speeds. Such precautions are air-water sprays or, still better, just water spray. There should be no lag between the time when the bur cuts the tooth and the time when the coolant reaches the bur. If there is insufficient water spray or if only an air coolant is used, severe pulp injury is most likely to occur.

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The high-speed instruments are designed to be used at light pressures, and operators are abusing them when they use too much pressure.

Dr. Robinson's presentation is summarized in the following paragraphs:

Injuries to the dental pulp produced by operative procedures usually are the result of thermal or chemical injury. Although mechanical trauma may affect the pulp directly, as in mechanical exposure or as a result of occlusal forces on a "high" restoration, mechanical injury to the hard structures most frequently is transmitted to the pulp as heat produced during operative procedures. It has long been recognized that heat can and does produce pulpal injury, if it is great enough and applied for a long enough time. Of course, the distance between the pulp and the point of application of the heat-producing agent is most important, the injury (that is, heat) at the pulp being inversely proportional to the thickness of the overlying dentine. When chemical injury occurs, it usually results from "sterilizing agents" and other caustics applied with good intent or from acids in cement used to aid in retention or as primary restorative materials.

The development of higher-speed rotating instruments and ultrasonic instruments for cavity preparation has renewed interest in pulpal pathology. Investigations have demonstrated that the use of water coolant, properly applied at the point of heat production, will reduce injury to the pulp to the degree of clinical insignificance, even with the highest speeds of rotation or vibration, but that any of the available methods of cavity preparation can produce injury if used improperly. In discussing pulpal injury from operative procedures, one must consider (1) the condition of the tissue, for the pulp may have been injured by disease processes or trauma before dental care was instituted and, as a sick pulp, it may not react in an adequate manner even to mild injury; (2) the method used and how it is used (properly or improperly); and (3) any other injurious agents that might be introduced.

Colonel Bernier's Summation as Moderator follows:

It may be seen from these reports that rotational instruments, particularly those in the higher speed ranges, may produce pulpal damage if injudiciously used. Of special significance is the knowledge that the kinetic energy produced is the force which is responsible for pulpal reactions. Although this was suspected in the past, it was only with the advent of high-rotational speeds that it could be shown. Analysis of the sound characteristics of these devices permits an extrapolation of data useful in assessing the effect of such kinetic energy upon the pulp tissue.

One may now state, as more than mere opinion, that (a) high rotational instruments can produce serious pulpal reaction, (b) greater care is required in their application, (c) a coolant must always be used, and (d) careful clinical analysis of the health status of the pulp is essential, since this is the biologic state against which the physical forces produced are directed.

THE ORAL PATHOLOGIST LOOKS AT THE PRACTICE OF DENTISTRY*

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I AM deeply appreciative of the opportunity to give this lecture—The Helen McClain Lecture of the American Academy of Oral Pathology.

Miss McClain is a native of Rockford, Illinois. As a registered nurse, she served in the Army Nurse Corps during World War I at Camp Grant, Illinois, and at Jefferson Barracks, Missouri. After the war she became secretary at the Rockford Municipal Sanitarium and then in the Pathology Department of St. Anthony's Hospital in Rockford. Miss McClain went to Washington and served first in the Surgeon General's Office and then in the Army Medical Museum, which now is the Armed Forces Institute of Pathology. In 1945 she was assigned as secretary to the director of the Division of Dental and Oral Pathology where, happily, she still is serving. With the founding of the American Academy of Oral Pathology, Miss McClain assumed the duties of special aide to the secretary, duties that she so well fulfilled without remuneration for eleven years. The Academy, to show its appreciation of Miss McClain's services, established this lecture which will be given yearly.

The successful practice of dentistry or any of its divisions depends upon fundamental basic knowledge, regardless of the manipulative skills involved. No matter how esthetically and technically perfect the structure is, it must fail if built on a foundation of mud.

The general practice of dentistry is comprised, for the most part, of prosthodontics, endodontics, and periodontics. I have purposely omitted oral surgery and orthodontics, for I believe that these two branches of dental practice require a great deal more graduate and special study than the general practitioner can devote to them, and few men in general practice deal with such problems. I may be taken to task for including periodontics in general practice, but I feel quite strongly that the well-trained and conscientious general practitioner can cope with the average periodontal lesion and can, in a very great measure, prevent it.

Dentistry has always been, and unfortunately still is, looked upon as a mechanical art. This is a misconception that has been handed down for over a century. Yet dentistry is no more purely mechanical than orthopedics or some phases of ophthalmology or gynecology. The insertion of a denture to

*The Helen McClain Lecture given before the American Academy of Oral Pathology in Minneapolis, Minnesota, April 19, 1959.

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restore function should no less be looked upon as a therapeutic procedure than the insertion of a vitallium replacement for the loss of the head of the femur, eyeglasses for the loss of a lens, or a pessary for the support of a uterus.

I believe that the reason for the mechanistic aura that has prevailed about the dentist is that it is generally felt that when one of our mechanical contrivances fails it is because of a lack of skill in its construction. This may be true at times, but many times it is not true. If the supporting tissues, mucosa and bone, are not healthy, no amount of mechanical perfection will render the replacement successful.

When the mucous membrane is affected through systemic derangement, it is the *entire* mucous membrane that is involved. The lesion that becomes clinically manifested simply represents a point of irritation. Eddy and Dalldorf have shown that maximum keratinization of vitamin-A-deficient animals occurred at the site of a placed irritant. It is also a well-known fact that evidence of scurvy is rarely, if ever, seen in edentulous areas (Fig. 1).

Fig. 1.—Scorbutic gingivitis. Note the severe inflammation of the gingiva about the teeth. In the upper central incisor region, where the teeth are missing, the tissue appears to be normal.

Atrophy of the oral mucosa is more prevalent than is probably realized and appreciated. It is of nutritional origin and is seen particularly in women in whom chronic blood loss through menstruation results in hypochromic, iron-deficiency anemia. Other causes of hypochromic anemia are a low intake of vitamin C and achlorhydria, factors that hinder the normal absorption of iron. Achlorhydria is frequently seen in middle-aged women at a time of life when dentures may be in demand.

Hypochromic anemia is rare in the male and, when present, is due to some lesion responsible for blood loss, such as hemorrhoids or a slowly bleeding ulcer of the gastrointestinal tract.

Squamous epithelium, if it is to remain in a healthy state, depends for a large part on adequate amounts of iron. When this element is deficient, the

epithelium becomes thin and atrophic and can ill stand any irritation. Atrophy of long standing can be the seat of neoplastic change, and carcinoma of the mouth and throat is known to supervene occasionally in patients with Plummer-Vinson's syndrome.

In the light of these facts, instead of condemning the prosthesis, as so many do, it would be wiser to investigate the nutritional and hematologic status of those who cannot tolerate their dentures.

As we have just noted, the cause of mucosal atrophy can be ascertained. However, there are many lesions of the oral mucous membrane in which the etiology is completely unknown. Into this group fall lichen planus, psoriasis, pemphigoid disease, and certain varieties of erythema multiforme. The tissues may not show any evidence of these conditions unless irritated or traumatized.

The lichenoid lesions that occur on the buccal and other surfaces of the mouth are focal manifestations of irritation in a previously prepared tissue. Sometimes they will appear shortly after the insertion of a bridge and, while the prosthesis undoubtedly incited the mischief, in a normal mucosa there would have been no untoward effect. Such tissue reaction can be likened to the "line of scratch" that the dermatologist employs in bringing out lichen papules on the skin.

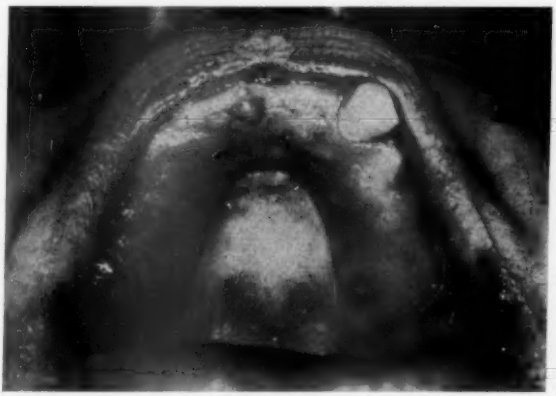

Fig. 2.—"Denture-sore mouth." In this case the denture was an acrylic one.

"Rubber-sore mouth" was the name given an entity characterized by a red, velvety, friable pattern of the denture on the mucosa. Many reasons were given for this condition, and the most popular of these was that the reaction in the tissue was due to sensitization to the vulcanite. Later, when acrylic dentures were made, a similar condition was found (Fig. 2). Metal bases caused the same picture. The relationship of allergy has never been satisfactorily proved.

I have histologically studied cases of this type and have been struck with the similarity of the microscopic picture to that of psoriasis. There were the

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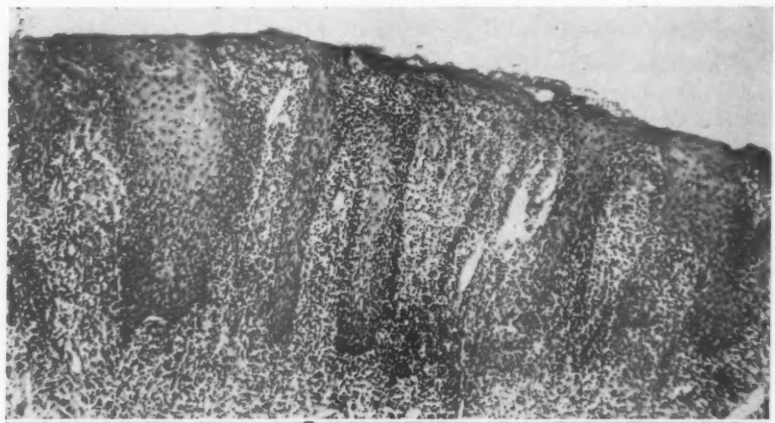
elongated test-tube-like papillae with the intervening atrophic epidermis (Fig. 3), and in some cases the characteristic microabscess of Monro could be seen (Fig. 4). The patients were often of the high-strung, tensive type that one associates with psoriasis.

Fig. 3.



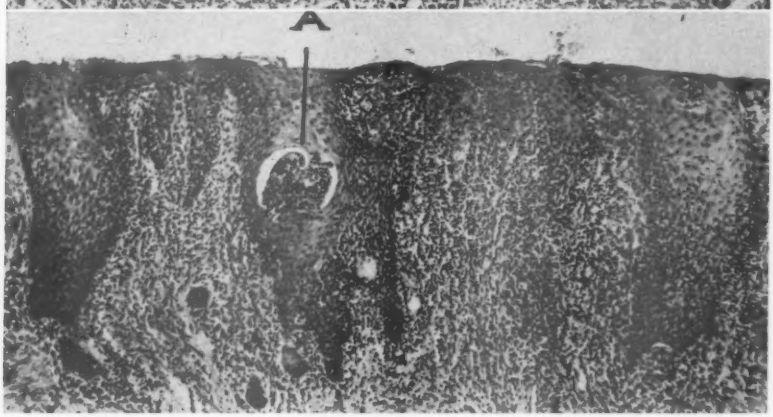


Fig. 4.

Fig. 3.—The test-tube-like elongations of the epithelial papillae and the atrophy of the interpapillary epithelium present a picture strikingly similar to that of psoriasis.

Fig. 4.—At *A* is seen an intraepithelial abscess of Monro.

Bone is influenced by systemic dysfunction. This apparently rigid structure is quite labile and sensitive to metabolic and many unknown factors. The use of affected bone for the support of prosthetic restorations must undoubtedly lead to trouble (Fig. 5). Diagnosis is of the utmost importance, and this can be correct only if one is trained in the pathology and roentgenographic interpretation of bone disease. Again, may I emphasize the importance of localization at a point of trauma, such as a tooth in traumatic occlusion, infection, or some other form of irritation. Twice I have encountered periapical

radiolucencies that proved to be giant-cell lesions of primary hyperparathyroidism. In the roentgenogram these were indistinguishable from banal periapical inflammations. In a case of multiple myeloma, a plasmacytoma

Fig. 5.—Active Paget's disease. The architecture of the bone is greatly altered and the trabeculae are aligned horizontally, a characteristic roentgenologic finding in the jawbone in Paget's disease. In this particular case, "mouth rehabilitation" was advised, a procedure that would have led to disaster. The patient had a number of the gross deformities of Paget's disease in addition to the roentgenographic trabecular pattern. All these signs were ignored.

Fig. 6.

Fig. 7.

Fig. 6.—Periapical localization of a plasmacytoma in a case of multiple myeloma. (Courtesy of Dr. H. Calman and the New York Institute of Clinical Oral Pathology.)

Fig. 7.—Resorptive localization about the premolar in Paget's disease. The tooth is vital; nonetheless, it was condemned because of the rarefied area.

developed about the apex of a tooth and could well have been mistaken roentgenologically for a granuloma or a radicular cyst (Fig. 6). In still another instance, an area of resorption in Paget's disease, which centered about the apex of a tooth, was considered to be an infective process and the tooth was condemned (Fig. 7).

A condition of bone that should be of great interest to the prosthodontist is the atrophy that is seen in older patients, particularly in women. The protein matrix of bone is formed by the osteoblasts which, in turn, are affected by stresses, strains, and hormones (particularly estrogen and to a lesser degree

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testosterone). The first two factors stimulate osteoblastic activity; the latter stimulates protein metabolism. These are often interrelated. A clear-cut entity is menopausal osteoporosis. When estrogen is withdrawn, the bones become thin, painful, and liable to compression or fracture. The spine and femoral head are most often involved, but I believe that we have lost sight of the fact that the jaws can be similarly affected. It becomes most marked in

Fig. 8.

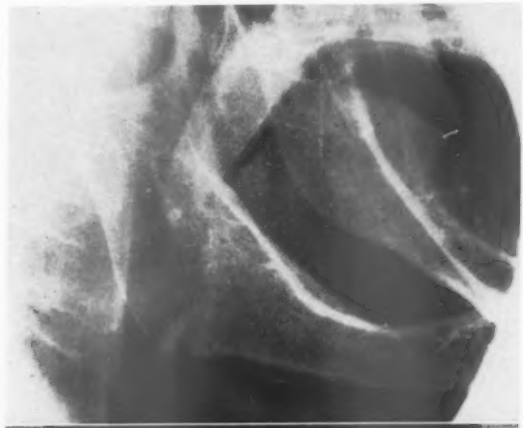

Fig. 9.

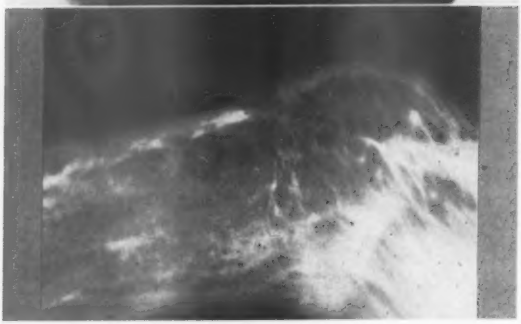

Fig. 8.—Extreme bone atrophy in a postmenopausal patient. She was unable to wear her denture and suffered greatly from atypical facial neuralgia.
Fig. 9.—Intraoral roentgenogram showing in greater detail the extreme atrophy.

the edentulous patients where functional stimulation is also missing (Figs. 8 and 9). The bones being painful, dentures become almost intolerable. This results in a poor food intake, with protein and other nutriment deprivation adding insult to injury. The jaws become more and more atrophic until the occlusal plain sinks beneath the floor of the mouth. In instances of this type the fitting of dentures becomes almost impossible and implants inimical. Osteoporosis should be recognized early and corrective measures should be instituted if prosthetic replacement is to be of any help.

Just as all periapical lesions are not caused by infection arising in the pulp canal, not all periodontal lesions are of local origin. The eosinophilic granuloma, for example, starting in the periodontal bone, may quickly destroy the supporting structure of the tooth, producing a roentgenographic picture that may be mistaken for an acute periodontal infection (Fig. 10).

Fig. 10.—Periodontal destruction caused by an eosinophilic granuloma.

Fig. 11.—Invasion of the supporting structure of the teeth by a carcinoma in the floor of the mouth.

One must always be on guard against excessive destruction of periodontal tissues, particularly that of short duration and in a localized area. Such a condition can be due to neoplastic invasion from a distant focus or to leukemic infiltration.

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It might be well here to consider the difference between a mobile tooth and a loosened tooth. This may seem to be an academic question of semantics, but I think that a differentiation in meaning may lead to a better diagnosis.

Fig. 12.

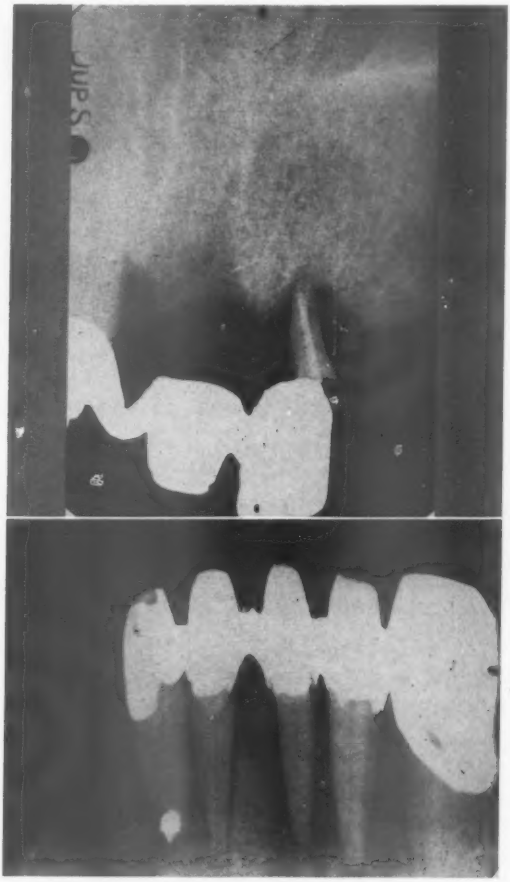

Fig. 13

Figs. 12 and 13.—Roentgenograms of some of the teeth of a 60-year-old man. These teeth had been under continual periodontal treatment for many years. An acute exacerbation drove him to one who told him that he must loose his teeth. After the acute episode had been controlled, the patient refused to heed this advice and returned to his former adviser for more periodontal treatment!

The mobile tooth may have its supporting structures still intact, but these may be so altered by disease that they are no longer efficient in firmly anchoring the tooth. The loosened tooth has its supporting structures destroyed and replaced by inflammatory, granulomatous, or neoplastic tissues (Fig. 11).

The mobile tooth is seen in both primary and secondary hyperparathyroidism, a disease that alters the structure of bone. Osteoporosis due to endocrine effects or protein depletion, brought about through excessive utilization as seen in pregnancy, hyperthyroidism, and diabetes also weakens the supporting structures of the teeth.

The interesting thing about the mobile tooth is that in the early stages of the condition there is no pocket formation. This is of significant diagnostic importance. Later the abnormal mobility, of course, may lead to opening the way to crevicular irritation and subsequent pocket formation. If the primary lesion that has led to the original mobility is not corrected, no amount of splinting, occlusal equilibration, or surgery will be helpful.

Fig. 14.—The patient was a 68-year-old man with hypertension and a high sedimentation rate. Some years before these teeth had been the seat of a very severe infection which had been controlled by antibiotics and by incision and drainage. The patient was so adamant about losing teeth that root therapy was done and the teeth were splinted. From time to time subacute exacerbations occurred, and one of the central incisors had to be removed. Finally the patient was told that there was no longer hope of salvaging his teeth. Still he refused extraction and sought someone who would consent to "save" the teeth. He found him. This roentgenogram was made some time after the completion of the "rehabilitation." It is to be noted that root resorption and periapical and periodontal disease still persist.

My discussion would not be complete without a word about the current practice of mouth rehabilitation. To try to restore aging teeth and jawbones to the physiologic and esthetic perfection of youth is unrealistic. Physiologic processes change with age, and tissues adapt themselves to these changes. I realize that the patient's resistance to the removal of teeth, no matter how diseased, is great. This is most marked in patients growing older, particularly in men. To them the loss of teeth is a form of castration and the wearing of full dentures represents the loss of youth. Pandering to their foibles and conceits at the expense of their health is to be strongly condemned (Figs. 12 and 13).

There is no doubt that in selected cases deranged oral function should be corrected in healthy patients. However, one should evaluate the patient as a whole and not consider just the local environment. The older patient with high blood pressure and degenerative changes certainly is not a fit candidate for the lengthy and disturbing procedures of mouth rehabilitation. Teeth

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that are markedly involved, either periodontally or periapically, should not be retained to serve as abutments simply because these teeth are the only ones available or to please a patient (Fig. 14). The specter of focal infection may be moribund, but it certainly is not dead.

In conclusion let me paraphrase Huxley:

"There can be no doubt but that the future of oral pathology and treatment, and therefore of dentistry in all its divisions, depends upon the extent to which those who occupy themselves with these subjects are trained in principles and impregnated with fundamental truths."

888 Park Ave.

ORAL ROENTGENOLOGY

American Academy of Oral Roentgenology

Arthur H. Wuehrmann, Editor

. . . . . .

THE INTERPRETATION OF TEMPOROMANDIBULAR JOINT ROENTGENOGRAMS

Nathan Allen Shore, D.D.S., New York, N. Y.*

TEMPOROMANDIBULAR joint roentgenography is essential in the establishing of an accurate diagnosis of temporomandibular joint dysfunction. The clinical findings that emerge in the course of a complete dental examination should be confirmed and corroborated by temporomandibular joint roentgenograms. When one approaches any case of temporomandibular joint disorder, from either the diagnostic or the roentgenographic angle, the fact that there are two interdependent joints that act in concert should be heeded.

Before the actual procedure is delineated, a brief discussion of the difficulties encountered in temporomandibular joint roentgenography should prove of value. The temporomandibular joint, because of its own innate complexity and because of its location in the skull in close proximity to other osseous structures, poses a challenge to the meticulous technician. Furthermore, variations in the angle of the x-ray beam, the position of the patient's head, and the position of the cassette complicate the problems of evaluation and comparison in the course of treating any case of pathologic occlusion. The efficacy and reliability of temporomandibular joint roentgenography depend directly upon the degree of success with which the practitioner meets these problems.[1-6]

The Oblique-Lateral Transcranial Projection.—The basic lateral views (oblique-lateral transcranial projection) of each joint should be taken with the patient's teeth clenched in the habitual convenience relationship, and a second one should be taken with the mouth wide open, so that the maxillary and mandibular teeth are separated as much as possible. The first of these views demonstrates the condyle-to-fossa relationship in the habitual convenience relationship; the second view demonstrates the position of the condyle, its relationship to the articular eminence, and the length and inclination of the path

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traversed by the condyle. Both of these views should be compared with comparable views of a normal joint, and any deviations from the normal should be carefully noted.[7, 8] These views are taken in the oblique-lateral transcranial projection (Fig. 1), which makes possible the most accurate demonstration of the joint structures in the lateral position.

The most noteworthy advantage of the oblique-lateral transcranial projection over a lateral roentgenogram parallel with the sagittal plane is the avoidance of the superimposition of other osseous structures upon the joint that is being x-rayed. As can be seen in Fig. 1, the cassette, *CD*, is at a 10 degree angle from the horizontal; *GH* forms a 10 degree angle with the vertical (*LM*); and the central ray of the machine, *JK*, is set at 15 degrees with the horizontal.

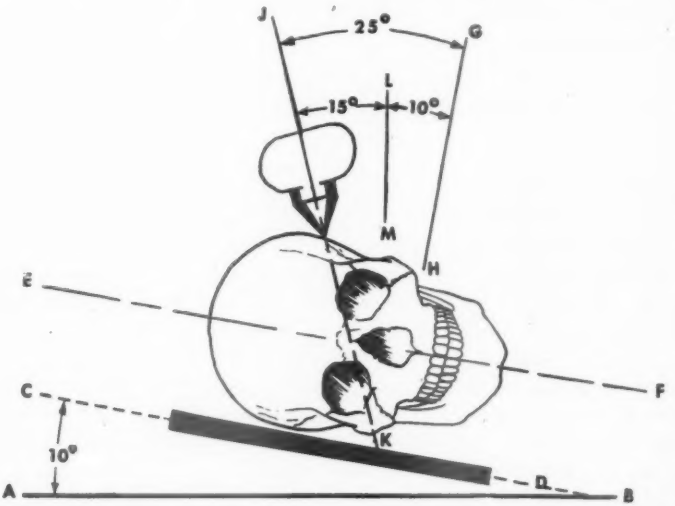


Fig. 1.—Principles of the oblique-lateral transcranial projection technique illustrating the attainment of the path of ray 25 degrees to the horizontal. (From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company, p. 181.)

Consequently, the basic principle of the oblique-lateral transcranial projection—namely, a 25 degree angle with the horizontal—is fulfilled. The details of the procedure for oblique-lateral transcranial projections are given in chapter 8 of my book. Alternative methods have been developed by Lindblom,[9] Grewcock,[10] Updegrave,[7] and Donovan.[11]

The primary purpose of lateral (oblique-lateral transcranial) roentgenography of the temporomandibular joint is to provide corroborative evidence of the clinical manifestations. Fig. 2 illustrates the oblique-lateral transcranial projection of normal right and left temporomandibular joints in the closed and open positions and should prove helpful for purposes of comparison. In the interpretation of such roentgenograms taken in the closed position, the first point is to note any differences that may exist between the left and right joints.

Next, using Fig. 2 as a comparative standard, one should check the floor of the glenoid fossa (*B*) for density, contour, irregularities, and defects. The density and contour of the articular eminence (*C*) are observed, and finally the joint gap or space (*F*) is studied. The condyle (*D*) should be centered within the fossa, so that an almost equidistant joint gap exists anteriorly, superiorly, and superoposteriorly between the condyle and the glenoid fossa, as can be seen in the upper section of Fig. 2. The left and right joint gaps should be compared,

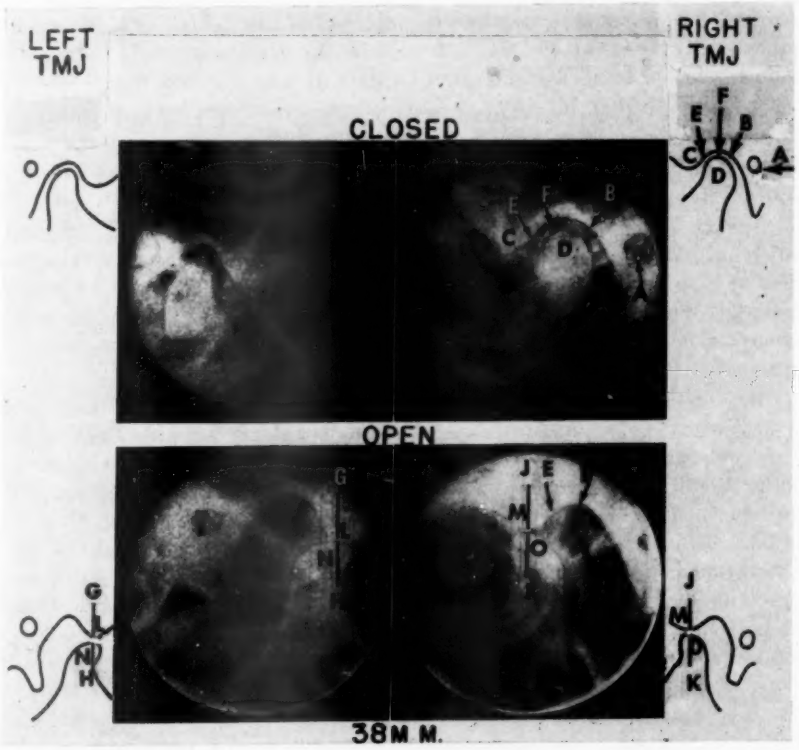


Fig. 2.—Temporomandibular joint roentgenograms of the left and right sides in the open and closed positions. *A*, External auditory meatus; *B*, glenoid fossa; *C*, articular eminence; *D*, condyle; *E*, posterior wall of the articular eminence; *F*, joint gap. Lines *GL* and *JM* traverse the centers of the left and right articular eminences, respectively; lines *NH* and *OK* traverse the centers of the left and right condyles, respectively.

and any irregularities or partial obliterations should be noted. The contour of the condyle (*D*) should be carefully examined for distortion or disharmony of shape, and any pathologic deformation or protuberances on the articular surfaces should be noted. The external auditory meatus is at *A*.

In an examination of the oblique-lateral transcranial projection in the open position (lower section of Fig. 2), the left and right joints should again be compared and any differences noted. The condition and shape of the floor of

the glenoid fossa, the articular eminence, and the angle of inclination of its posterior wall (*E*) and the condyle should be checked. The joint space between the articular eminence and the condyle and the relationship of the center of the condyle to the center of the articular eminence (*H* to *G* and *K* to *J*) should be noted. Finally, the distance the condyle has traveled from the closed to the open position and the possible unilateral excursion of the mandible should be observed.

The existence of a state of hypermobility of the condyle is confirmed when the roentgenogram shows that the center of the condyle (depicted by the line *NH* or *OK*) has passed moderately anterior to the center of the articular eminence (depicted by the line *GL* or *JM*) to a state of partial dislocation (subluxation) or markedly anterior to a state of true dislocation.

Hypomobility of the condyle will be visualized roentgenographically by the limited movement of one or both condyles in the open position; this is measured by the distance between the condyle center and the center of the eminence (*H* to *G* and *K* to *J* in Fig. 2).

Among other data to be uncovered from oblique-lateral transcranial projections are developmental defects, calcific deposits, fractures, ankyloses, areas of osseous rarefaction and condensation, bone pathology, and traumatic injuries. When treatment splints are being used for restoration of vertical dimension,[12, 13] lateral roentgenograms are of value in evaluating the degree of progress.

Because of the absence of the dimension of depth, which lies in the direction of the central ray, movements along the line of that ray are either not recorded or are mistakenly evaluated. For example, mediolateral condylar movements in the line of the central ray may be incorrectly interpreted as movements in the superior-inferior direction, since both directional movements register similar profiles. This is schematically represented in Figs. 3 and 4. In Fig. 3, *b* represents a mediolateral view of a normal right temporomandibular joint, and *a* represents a projected view on a film of the same joint at a 25 degree angle to the horizontal. The angle of the ray is 25 degrees, and the x-ray line (*ADB*) is parallel with the lateral slope of the condyle and the floor of the glenoid fossa *E*. When this projection is superimposed on the film (*F*) as *CB*, the joint gap is seen at *G*, the floor of the glenoid fossa is at *E'*, and the condyle is in its normal position. The lateral slope of the condyle (*D* of drawing *b*) is labeled *M'* in drawing *a*.

Fig. 4, *b* represents a composite mediolateral view of both a normal and an abnormal right temporomandibular joint. As in Fig. 3, *D* (the solid line) depicts the position of the condyle, but now *D* represents a condyle that has shifted medially and *D'* the imaginary position of a normal condyle. Again, as in Fig. 3, the angle of the ray is 25 degrees and the x-ray line (*ADB*) is parallel with the lateral slope of the condyle and the floor of the glenoid fossa *E*. *ADB* produces joint gap *G* on the film *F* in *I*(*A*). Contrast this depiction with the imaginary projection *A'D'B'* and its result, joint gap *G'* in II(*a*). According to the roentgenogram I(*a*) on film *F*, the condyle is in an inferior position. However, by careful study of diagram *b* (solid line *D*), it becomes apparent that

a medial position of the condyle without any change in vertical position will be depicted as an inferior position on the film. In other words, a condyle that is positioned medially and one that is positioned inferiorly will produce similar roentgenograms. This two-dimensional concept of a three-dimensional structure applies to all roentgenograms.

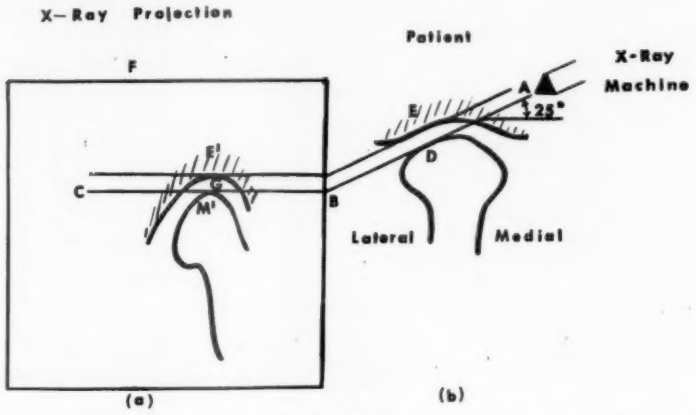


Fig. 3.—Diagram of the lateral-oblique transcranial projection of a normal temporomandibular joint of a patient *(b)* and the resulting projected view *(a)* on a film. (After Norgaard. From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

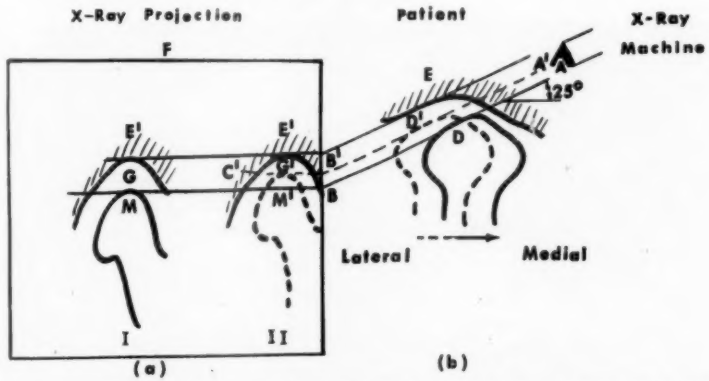


Fig. 4.—A medial shift of the condyle (solid line) in *B* and its resultant projection in *A*. *I*, The normal condyle (dotted line) in *b* and *a*. *II*, Illustrated for comparison. Compare *G* and *G'*. A medial movement in *b* (solid line) is misinterpreted as an inferior movement. (After Norgaard. From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

Consequently, the possibility of such a roentgenographic misinterpretation should alert the painstaking practitioner to the danger of making diagnoses solely on the basis of oblique-transcranial roentgenographic studies. For the precise and comprehensive investigation into the physiology and relative positions of the component parts of the temporomandibular joint, an additional view,

which supplies the third dimension of depth to the oblique-lateral transcranial projection, is necessary. This is a mediolateral view and can be regarded as a modified posteroanterior exposure.[13-17]

The Midorbitomeatal-Base Line, Corner-of-the-Mouth Projection.—This projection, based on the work of Waters and Waldron,[18] Whitehouse,[19] and Shore,[20] permits a simultaneous mediolateral view of the floor of the glenoid fossa, the joint gap, and the condyle of the right and left temporomandibular joints in the closed position on the same film. The rationale of the technique is illustrated in Fig. 5. The midpoint of the orbitomeatal base line (AB), which extends from the outer canthus of the eye to the superior border of the external auditory meatus, is *C*. With a flexible ruler and skin pencil, a line is drawn from the corner of the mouth (*R*), through *C*. The extension of this line (*CR*) creates the angulation for the central ray.

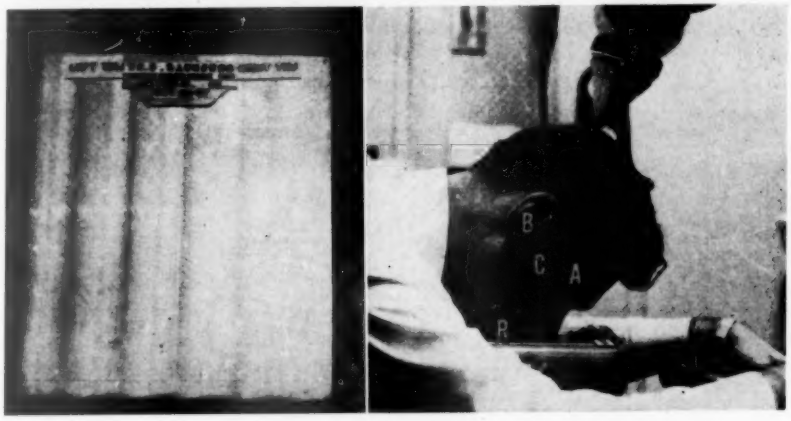
Fig. 5.—Principle of the technique of the midorbitomeatal-base line, corner-of-the-mouth projection. (After Whitehouse. From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

Fig. 6, *A* shows the cassette fastened to the headrest, with the pertinent data placed at the top of the cassette. The cassette is placed parallel to the floor with the aid of a level. The patient, protected by a lead apron and seated on a stool, as in *B*, is instructed to clench his teeth, with nose and chin touching the center of the cassette and both arms extended on the armrests of the dental chair. The x-ray machine is adjusted so that the central ray traverses the line *CR*. The patient is told to hold his breath while the film is exposed. The exposure factor is 65 kv. at 15 Ma. for three seconds, at an 8 inch distance with an aluminum filter 1 mm. thick.

The mediolateral, closed-position views of both temporomandibular joints on a single film enable the practitioner to investigate the relationships of the

component structures in an additional third dimension not possible in the lateral views.

Fig. 7 shows a roentgenogram of the right and left temporomandibular joints produced by the midorbitomeatal-base line, corner-of-the-mouth projection.



a. *b.*

Fig. 6.—*a*, The fastening of the cassette and the placement of the identifying data are illustrated. *b*, The placement of the patient's head and arms and the angulation of the central ray to the marked lines on the face are illustrated (refer to Fig. 5). (From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

Fig. 7.—Roentgenogram of normal left and right temporomandibular joints produced by the midorbitomeatal-base line, corner-of-the-mouth projection. *A* and *B* indicate the left and right joint gaps. The distances between the lines *C* and *D*, and *E* and *F* represent lateral shifts of the condyles, when present. (From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

The temporomandibular joints are in the closed position in this posteroanterior projection (see Figs. 5 and 6). The outstanding contribution of this projection is the direct visualization of the relationship between the condyle and the glenoid

fossa in the mediolateral view, making possible the observation of any mediolateral movement. Lateral shifts of the condyles would be evident by disparities in the distances between *C* and *D* and between *E* and *F* in Fig. 7. This medio-

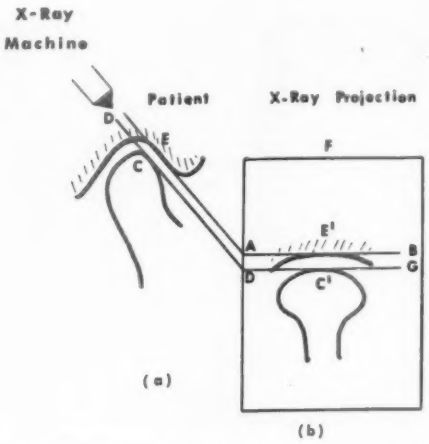


Fig. 8.—Diagram of the midorbitomeatal-base line, corner-of-the-mouth projection of a normal-positioned temporomandibular joint of a patient *(a)* and the resultant projected view *(b)* on a film. (From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

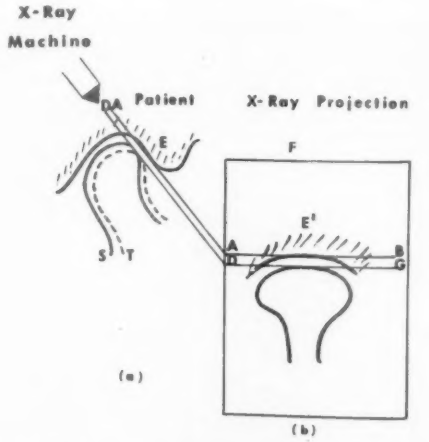


Fig. 9.—A superior position and an anterior position of a patient's condyle is shown in *(a)* and the similar projection that they both can give on the film is shown in *b*. The projection of the normal condyle level is shown as *DG*. (From Shore, N. A.: Occlusal Equilibration and Temporomandibular Joint Dysfunction, Philadelphia, 1959, J. B. Lippincott Company.)

lateral projection also affords the practitioner the opportunity to observe the joint gap between the posterior wall of the articular eminence and the condyle, the mediolateral contour and density of the posterior wall of the articular

eminence and of the condyle, and a mediolateral aspect of the coronoid process. Osseous changes in the temporomandibular joints, mandible, nasal and malar bones, zygoma, zygomatic arches, and antra are also visualized in this view.

Fig. 8, *a* shows a normal right temporomandibular joint in the midorbitomeatal-base line, corner-of-the-mouth projection, and the resultant film projection is shown in Fig. 8, *b*. The x-rays, passing parallel to the posterior wall of the articular eminence *E*, and the anterior surface of the condyle *C*, produce projection lines *AB* and *DG*, respectively, on the film *F*. The space between *AB* and *DG* is the projected joint gap. Fig. 9 shows how dissimilar condylar positions can produce similar images on the x-ray film. The solid-line condyle *S* denotes a normal position. The dotted-line condyle *T* demonstrates an inferoanterior position with respect to the normal. As in Fig. 8, the x-ray beam *AD*, parallel to the posterior wall of the articular eminence *E*, produces line *AB* on the film, with E' as the articular eminence. The superior position of condyle *S*, and the inferoanterior position of condyle *T* are similarly projected on the film as *DG*. These positions produce joint gaps that are narrower than normal. By the same reasoning, an inferior or posterior position of the condyles will produce identical x-ray images and joint gaps that are larger than normal.

It becomes apparent, then, that any one x-ray projection, taken by itself, can lead to gross diagnostic misinterpretations. For precise and accurate orientation of the condyle in the glenoid fossa, both oblique-lateral transcranial and posteroanterior projections are essential. Interpreted in conjunction with one another and as correlative proof of clinical findings, these roentgenographic procedures should be valuable adjunets in the treatment of temporomandibular joint dysfunction.

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ROENTGENO-ODDITIES

Multiple Dens in Dente

Dens in dente is not an uncommon finding during routine roentgenographic examinations. These developmental anomalies can be of a coronal or radicular form. The coronal form can vary from an overly deep pit to a complete invagination of the enamel and dentine throughout the entire length of the pulp. The most common site of this condition is the lingual pit of the maxillary lateral incisors, and its greatest significance is in the potential bacterial invasion of

the pulp via this route. The case shown here was rather odd in that not only were all four first premolars involved, but one tooth possessed two of these defects. The reproduction of one of the bitewing roentgenograms shows the

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Each month this section will bring to the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY one or more roentgenograms which demonstrate unusual, unexpected, rare, or bizarre roentgenographic changes. These roentgenograms will be accompanied by an explanation or by words of inquiry, regarding the particular change. All films used in this section will be accepted with the understanding that 2 by 2 or 3¼ by 4 inch slides or glossy photographs of the films will be made available to interested readers through the editor of the American Academy of Oral Roentgenology at the individual's expense. The cost will involve only the photographer's charges. Each slide or print will give credit to the donor. Interesting roentgenograms are solicited from all sources. Please be certain to identify your films properly so that they can be returned. All material for publication should be submitted to Dr. Arthur H. Wuehrmann, University of Alabama School of Dentistry, Medical Center, Birmingham, Alabama.

double dens in dente in the upper first premolar and an amalgam restoration placed in one of the occlusal pits of this tooth. The roentgenopaque enamel lining the invaginations is clearly seen in this roentgenogram. Note that while the invaginations are very small occlusally, they are rather large within the pulp and have even caused the outer contour of the tooth to bulge outward in this area. The diagnosis of dens in dente in this case was made possible by roentgenographic examination.

Lincoln R. Manson-Hing,
University of Alabama.

ENDODONTICS

The American Association of Endodontists

Captain Warren J. Hedman, Editor

THE INCIDENCE OF BACTEREMIA IN ENDODONTIC MANIPULATION

Preliminary Report

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Philadelphia, Pa.

ENDODONTIC procedures have been under criticism by certain members of the profession for a long time, particularly as related to focal infection. Many still believe that pulpless teeth, especially those with an area of rarefaction, are a focus of infection which ultimately could produce a focal infection. The elimination of this possible focus of infection by conservative endodontic methods has been and still is questioned. Exodontic procedures, on the other hand, have never been censored. It is believed that removal of the tooth eradicates the focus and thereby eliminates the complication of a metastatic or focal infection.

We should like to offer evidence that proper endodontic procedures can produce less likelihood of focal infection than exodontic procedures.

It has been demonstrated clinically and experimentally that focal infection can develop as a result of a bacteremia[1] following extraction of teeth. The incidence of bacteremia as a result of exodontic and periodontal manipulation has been reported by numerous investigators.[2-7] In the extraction of teeth, it has been shown that heavy trauma invariably produces a greater dispersal of microorganisms into the blood stream from the original focus. Therefore, the reduction of trauma can curtail the number of bacteria that enter the blood

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***Clinical Assistant, Albert Einstein Medical Center, Northern Division.

stream and thus prevent the complication of the development of certain organic diseases, particularly the dread subacute bacterial endocarditis in patients who have a history of rheumatic heart disease.

Investigations of the relationship of endodontic procedures to bacteremia are very meager. Robinson and his group[5] did not detect the presence of bacteria in the blood in seven cases following reaming procedures and filling of the root canals. They did not state how many of each were done and whether or not cultures were taken of the root canals to determine the presence of microorganisms. In all instances they used the rubber dam. While many laboratory procedures were discussed, specific procedures for this series of cases were not given. Beechen and his group[8] found no evidence of positive blood cultures in pulpotomy procedures in one permanent molar and twenty-two deciduous molars. Their patients ranged in age from 4 to 11 years. The coronal portion of the pulp was cultured, and the organisms were identified in each case. They were able to obtain a 10 ml. sample of blood in their young patients. Ross and Rogers[9] treated six cases and found that in three cases of vital extirpation blood cultures were all positive, while in three cases of necrosis of the pulp they were all negative. They explain that the positive blood cultures were due to the organisms being carried into the blood stream through the pulpal circulation by means of the broaches and reamers as they traversed the infected portion of the carious process in the coronal portion of the pulp. The three cases of necrosis of the pulp produced negative cultures because there was no pulpal circulation to propel the bacteria into the blood stream. They did not take cultures of the coronal portion or root canals of the teeth tested.

The following study was done to determine whether or not endodontic procedures can produce a bacteremia. If no bacteremias or a smaller incidence of bacteremias occur following endodontic procedures as compared to exodontic procedures, endodontics may be the treatment of choice, particularly for patients with valvular heart disease.

CLINICAL MATERIAL

Fifty patients, ranging in age from 19 to 78 years, were chosen at random from the outpatient clinics of the Albert Einstein Medical Center. Only teeth in which endodontic manipulation such as reaming and filing could be performed were used, and only patients who had received no antibiotics or sulfonamides within one month prior to manipulation were selected.

Patients were divided into two groups: Group A (twenty-six cases), in which endodontic manipulation was done only within the confines of the root canal, and Group B (twenty-four cases), in which the endodontic manipulation was purposely done beyond the confines of the root canal. Both groups were classified as to vital and nonvital pulps.

PROCEDURES

Bacterial cultures were made from root canals with paper points which were then suspended in brain-heart infusion broth. The cultures were taken

immediately after manipulation, and the microorganisms were identified. Cases that exhibited negative root canal cultures were discarded from the study.

The tooth was isolated with cotton rolls. Aseptic precautions in the use of rubber dam and sterilization were not exercised. This was purposely done to increase the number of microorganisms in the root canal that ultimately may gain entry into the blood stream. In each case the reamer or file was moved vigorously with a pumping motion for ten minutes.

Blood Samples.—Blood samples (16 ml.) were collected before, immediately after, and ten minutes after endodontic manipulation. Each of the 16 ml. blood samples were divided into four aliquots, so that 4 ml. of blood was deposited into each flask containing 20 ml. of brain-heart infusion broth. Sodium polyanethol-sulfonate (Liquoid), 0.033 per cent, was added to the broth to neutralize in vitro phagocytic activity of the blood and to prevent coagulation.[11] This drug does not interfere with bacterial multiplication in brain-heart infusion broth. The blood cultures were incubated at 37° C. for two weeks, and the organisms were identified.

RESULTS

All preoperative blood samples taken immediately before endodontic manipulation were negative for growth. Blood samples taken immediately after manipulation were positive in six out of fifty cases, an incidence of 12 per cent. Blood samples taken ten minutes later exhibited no growth. (See Table I.)

TABLE I. INCIDENCE OF BACTEREMIA FOLLOWING ENDODONTIC MANIPULATION

PROCEDURE	NO. OF CASES	IMMEDIATELY AFTER MANIPULATION		TEN MINUTES AFTER MANIPULATION	
		NO. POSITIVE	PER CENT POSITIVE	NO. POSITIVE	PER CENT POSITIVE
Group A					
Within root canal	26	0	0.0	0	0.0
Group B					
Beyond root canal	24	6	25.0	0	0.0
Total	50	6	12.0	0	0.0

In Group A, in which instrumentation was done within the confines of the root canal, only one blood culture out of twenty-six cases was positive. This one can be considered as a contaminant, since the organism isolated from the blood culture flask was not present in the root canal. The bacteria that were present in the root canal of this case were the *Streptococcus viridans* and *Bacillus subtilis,* while the organism that was recovered from the blood stream was *Staphylococcus albus nonhemolyticus.*

In Group B, in which manipulation was performed beyond the apex of the root canal, six out of twenty-four cases, or 25 per cent, were positive for growth in the blood culture flasks. They were positive in both vital and nonvital cases (three vital and three nonvital). (See Tables I, II, and III.)

In the ten-minute blood samples all blood cultures were negative in both groups, with one exception. This exception can be considered a contaminant since it was negative in the before- and immediately-after-manipulation

TABLE II. INCIDENCE OF BACTEREMIA IN VITAL AND NONVITAL CASES

	NO. OF CASES	NO. POSITIVE	PER CENT POSITIVE
Vital	35	3	8.5
Nonvital	15	3	20.0
Total	50	6	12.0

samples. Also, the organism that was recovered was a micrococcus that was not present in the root canal.

The total number of positive blood cultures in both groups was six out of fifty cases, or 12 per cent. The bacterium that was recovered in four instances was the *Streptococcus viridans.* Twice the *Str. viridans* was isolated alone, and

TABLE III. THE EFFECT OF ENDODONTIC MANIPULATION BEYOND APEX UPON THE INCIDENCE OF BACTEREMIA*

PATIENT	ROOT CANAL CULTURE	TOOTH INVOLVED	BLOOD CULTURE RESULTS							
			IMMEDIATE FLASKS				TEN MINUTE FLASKS			
			A	B	C	D	A	B	C	D
M. D.	1, 6	# 9 Vital	1	1	1	1, 6	0	0	0	0
M. K.	1, 5, 6	# 4 Nonvital	1	0	1	0	0	0	0	0
H. A.	1, 2, 5, 7	# 6 Chronic abscess, fistula	1	1, 6	1, 6	1, 6	0	0	0	0
R. W.	1, 5	# 12 Vital	1	1	0	1	0	0	0	0
E. R.	1, 6	# 9 Vital	6	0	0	0	0	0	0	0
C. M.	1, 5, 6	# 6 Nonvital	0	0	6	0	0	0	0	0

Number indicates the identified bacteria, see Key in Table IV.

# indicates tooth treated.

*Only the six positive cases are shown. The remaining forty-four cases are deleted; they are all negative with the exception of two cases that exhibited contamination.

twice it was recovered mixed with diptheroids. In the other two cases, diphtheroids were recovered from the blood cultures. In all the blood cultures the bacteria recovered from the blood were present in the root canals. Blood cultures demonstrated the presence of bacteria in more than one flask four times. Twice it was present in only one flask. This is indicative of the small number of bacteria that are dispersed into the blood stream.

TABLE IV. ORGANISMS ISOLATED FROM THE ROOT CANALS

Key	
1—*Streptococcus viridans*	(37)
2—*Streptococcus nonhemolyticus*	(8)
3—*Diplococcus pneumoniae*	(2)
4—*Staphylococcus albus hemolyticus*	(9)
5—*Staphylococcus albus nonhemolyticus*	(24)
6—*Diphtheroids*	(16)
7—*Neisseria* (*flava*, *sicca*, *catarrhalis*)	(16)
8—*Streptococci B hemolyticus*	(2)
9—*Micrococcus*	(5)
10—*Bacillus coli*	(1)
11—*Bacillus subtilis*	(1)
12—*Staphylococcus aureus*	(1)

Number in parentheses indicates the number of times the organism was recovered from the root canals. The other number indicates key that is used in Table III.

The types of organisms found in the root canals are listed in Table IV. Most of the bacteria isolated from the root canals were mixed cultures. This may be indicative of salivary contamination of the root canals. In only six out of fifty cases were single strains of bacteria found in the root canals; this was the *Str. viridans.* In all others, mixed microorganisms of from two to five different varieties were found. The streptococci were isolated in forty-one out of fifty root canals. Other microorganisms were isolated with lesser frequency. Two cases exhibited no growth, and these were discarded from the study.

DISCUSSION

Numerous investigators have shown that one of the most important factors in the production of a bacteremia is the degree of trauma. The ruptured blood vessels and the number of bacteria at the manipulative site influence the number of bacteria that enter the blood stream. Our results indicate that of all the dental procedures—exodontics, periodontics, and endodontics—the latter is least likely to cause a bacteremia. The area of manipulation in the root canal is small and limited. Comparatively, the number of blood vessels and capillaries that can be opened to bacterial entry is much less than in the extraction of teeth or in periodontal manipulation. Moreover, the number of organisms that can be introduced is limited. Endodontic procedures are usually done under rubber dam by a surgically clean technique; thus, the possibility of introducing large inocula into the blood is reduced. In the other procedures, more numerous blood vessels are opened and a larger number of bacteria could enter the circulation.

In this investigation we did not use aseptic precautions or rubber dam. This had the effect of introducing more microorganisms or a larger inoculum. Despite this procedure, the incidence of bacteremia in Group A was zero, while in Group B the incidence was 25 per cent.

In this series 16 ml. of blood was used for aerobic study, whereas in the exodontic series an 8 ml. sample of blood was used. Anaerobic methods of culturing were not utilized in this study. It was found in our previous studies[11] that anaerobiosis did not enhance our blood culture results. It did, however, increase the detection of different types of bacteria. Only once in over 300 cases was there a positive growth under anaerobic conditions that was negative under aerobic conditions. We felt that in this study we could increase our percentage of positive cultures if we cultured the 16 ml. blood sample under aerobic conditions.

In a previous investigation we found that the incidence of bacteremia following the removal of teeth was 84.9 per cent. Moreover, if the bacteremia was analyzed as to the degree of trauma, it was found that mild trauma produced an incidence of 68.7 per cent, whereas heavy trauma produced an incidence of 93.4 per cent. In this investigation endodontic manipulation produced an incidence of only six out of fifty cases, or 12 per cent. If the endodontic results are analyzed on the basis of trauma, such as manipulating within or beyond the confines of the root canal, the results are even more striking. In

the cases in which the manipulation was done within the confines of the root canal, comparable to mild trauma, none were positive. Manipulation beyond the confines of the root canal, such as perforating the apex, comparable to heavy trauma, produced an incidence of six out of 24 cases, or 25 per cent (Tables V and VI). Kennedy and his associates,[12] working on monkeys, also showed that

TABLE V. COMPARATIVE INCIDENCE OF BACTEREMIA FOLLOWING EXODONTIC AND ENDODONTIC PROCEDURES

		IMMEDIATELY AFTER PROCEDURE		TEN MINUTES AFTER PROCEDURE	
PROCEDURE	NO. OF CASES	NO. POSITIVE	PER CENT POSITIVE	NO. POSITIVE	PER CENT POSITIVE
Exodontic	93	79	84.9	41	44.1
Endodontic	50	6	12.0	0	0

bacteremias were produced when hemolytic streptococci were placed in the root canal only if the apical tissues were traumatized. The comparative ten-minute results were also striking. No positive cultures were exhibited in Series A and B. This is indicative that the number of bacteria entering the blood stream was so small that they could not be detected at the end of ten minutes.

Proof that the instrument was manipulated beyond the apex was confirmed in two ways. In a group in which endodontic therapy was carried to completion, x-rays demonstrated the position of the file beyond the apex. In the group in which no further therapy was performed, the tooth was extracted with definite visualization of the instrument beyond the apex.

TABLE VI. THE EFFECT OF TRAUMA ON THE COMPARATIVE INCIDENCE OF BACTEREMIA IN EXODONTICS AND ENDODONTICS

		IMMEDIATELY AFTER PROCEDURE		TEN MINUTES AFTER PROCEDURE	
PROCEDURE	NO. OF CASES	NO. POSITIVE	PER CENT POSITIVE	NO. POSITIVE	PER CENT POSITIVE
Exodontic					
Trauma I	32	22	68.7	11	34.3
Trauma II	61	57	93.4	30	49.2
Endodontic					
Within confines	26	0	0	0	0.0
Beyond confines	24	6	25.0	0	0.0

While it may be anticipated that vital pulps with a blood circulation present would produce a higher incidence of bacteremia than necrotic pulps, our results showed no difference. The pulpal circulation is such that the number of blood vessels or capillaries that exit from the pulp is exceedingly small. In the pulp there are numerous capillaries, but there is no collateral circulation. Vessels do not communicate or anastomose with the circulatory system outside the pulp. The circulation of the pulp is like a pocket of capillaries that has one, two, or four veins as a route of exit. Therefore, the number of bacteria that could gain entry into the circulation through the pulp becomes markedly reduced.

In vital and nonvital cases manipulation within the confines of the root canal may push bacteria beyond the root apex but not necessarily into the circulation. Manipulation beyond the apex can force microorganisms directly into the blood stream and into the bone marrow spaces. This has the effect of introducing the bacteria into a closed circulatory system by injecting them directly into the circulation.

Despite the fact that the bacteria were introduced directly into the blood stream, the number of positive cultures was small. This may be attributed to the fact that the number of bacteria that could be introduced with reamers or files is so small that they could not be detected when 16 ml. of blood was cultured. Perhaps larger blood samples could increase the number of positive blood cultures.

The results of this investigation are very important from the standpoint of clinical application. They suggest that techniques of manipulation should be done within the confines of the root canal to prevent a bacteremia which can produce a focal infection. The results also purport to show that endodontics is a safer procedure than the removal of teeth, even if manipulation is performed beyond the apex.

In treating patients with a history of valvular heart disease, it is best to select a procedure that is least likely to produce a bacteremia. In such patients, therefore, endodontics should be the treatment of choice whenever possible. The procedure should be such that the reaming and filing are done with utmost care to prevent perforation of the apex.

Despite the fact that the incidence of bacteremia is reduced in endodontic procedures and is not demonstrable if the manipulation is confined within the root canals, patients with a history of valvular heart disease should be premedicated with parenteral antibiotics. Premedication does not mean that instrumentation can be done with careless abandon. The selection of a more conservative approach with prophylactic antibiotic therapy reduces the risk of the development of the dread disease, subacute bacterial endocarditis, and gives such patients the maximum protection. So far no case of subacute bacterial endocarditis has ever been reported following endodontic treatment.[10]

SUMMARY

The incidence of bacteremia following vigorous filing for ten minutes under nonsterile conditions was 12 per cent in fifty cases.

If the manipulation was kept within the confines of the root canal, there was no demonstrable bacteremia in twenty-six cases.

Of twenty-four cases in which manipulation was purposely done beyond the apex of the canal, six (25 per cent) displayed positive blood cultures.

Bacteremias were manifest in both vital and nonvital cases (three in each).

Blood samples taken ten minutes after endodontic manipulation revealed no positive blood cultures in the fifty cases.

For patients with a history of valvular heart disease, endodontics should be the treatment of choice whenever possible.

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THERAPY OF THE ENDODONTICALLY AND PERIODONTALLY INVOLVED TOOTH

Report of a Case

Samuel R. Rossman, D.D.S., Bernard Kaplowitz, D.D.S.,** and S. Robert Baldinger, D.D.S.,** Philadelphia, Pa.*

PROGNOSIS for the successful treatment of a tooth that is both endodontically and periodontally involved has long been considered poor by leading authorities in these fields. A review of the literature reveals very little other than a poor prognosis and advised extraction for any teeth so involved. This is especially true in the case of a deep periodontal pocket which communicates either directly or by a fistulous tract with a periapical lesion.

For some time we have felt that these teeth might lend themselves to successful therapy if close coordination between the endodontist and the periodontist could be established. Such a case, successfully treated, is here reported.

CASE REPORT

The patient, a 23-year-old man, was in good health. He complained of slight swelling of the gingiva about the mandibular left first molar. He also said that the tooth felt loose and slightly tender during mastication. Examination showed a very clean and generally healthy mouth, free of caries. The alveolar mucosa over the mandibular left first molar showed a soft, fluctuant swelling. Pressure elicited pus from the gingival crevice. A roentgenogram (Fig. 1) revealed disruption of the lamina dura and a large, diffuse periapical area of rarefaction around the distal root of the tooth. Radiolucency indicative of an incipient resorptive process at the interradicular alveolar crest was also noted, as well as thickening of the periodontal membrane space around the apex of the mesial root and an overhanging distal margin on the restoration in this tooth.

Periodontal examination revealed a pocket on the buccal surface, extending directly into the bifurcation the depth of the entire periodontal probe but not perforating through to the lingual surface. A gutta-percha point was placed in the gingival crevice, gently inserted to the point of resistance, and radiographed (Fig. 2). The pocket depth on the mesial and distal surfaces was 4 and 5 mm., respectively.

The occlusion revealed a premature contact in the centric pathway on the tooth involved, with a marked anterior glide of the mandible into final closure. No general pattern of occlusal attrition was obvious, and there was no history of tensional habit patterns, such as bruxism.

The periodontal therapy described in this article was performed in the Henry B. Robinson Clinic for Surgical Research in Periodontics, University of Pennsylvania, School of Dentistry.

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Mobility of this tooth was 1 degree. The medical history was essentially negative and noncontributory to the existing localized periodontal and endodontic problem.

A vitality test with a Burton Vitalometer elicited no response. The diagnosis was chronic alveolar abscess communicating directly with an infrabony periodontal pocket.

Fig. 1.

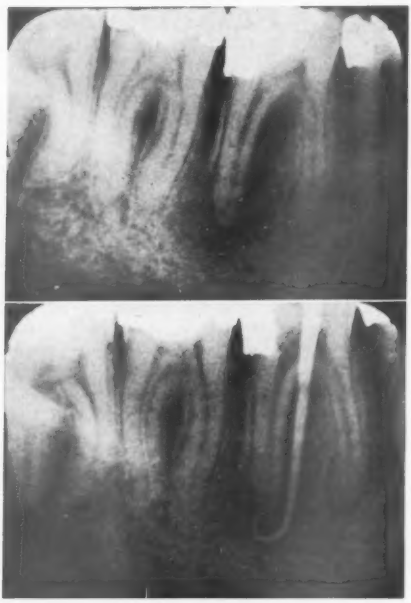

Fig. 2.

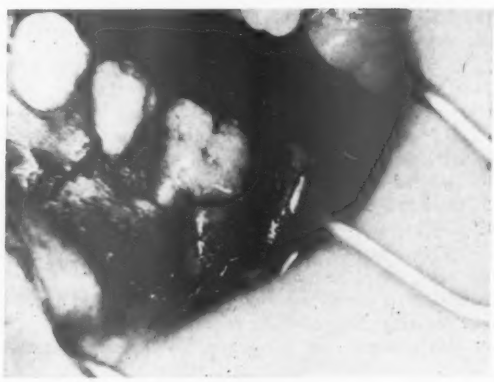

Fig. 3.

Fully realizing the very questionable prognosis and the desire to avoid disrupting the continuity of the arch in a young person, we decided upon an attempt to treat rather than extract after the patient was made aware of the poor prognosis.

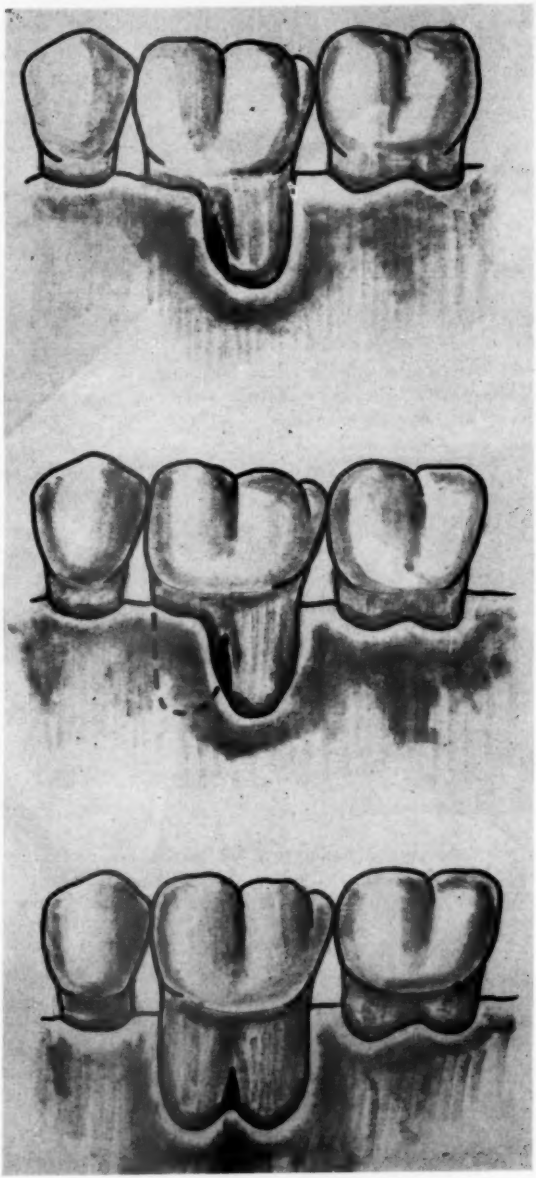

Fig. 4.

In view of the direct communication between the periapical and the gingival lesions, it was felt that the first step should be thorough biomechanical instrumentation of the canals. After this was done, a polyantibiotic (P.B.S.C.) was placed in the canals and the tooth was sealed. The rationale governing this first step was that it was important to remove any pathogenic organisms present in the canals plus all of the damaged and necrotic tissue. If this were not accomplished, the toxic by-products of bacterial metabolism and organic decomposition might interfere with any attempt to induce healing.

Periodontal therapy was now instituted. Under local anesthesia, a vertical incision on the buccal side was made from the gingival margin at the midline of the first premolar into the alveolar mucosa. The gingiva distal to this incision was freed and the entire buccal tissue, including the periosteum, was reflected, thus giving access to the involved area.

Probing and visual examination indicated that this was an infrabony pocket with three osseous walls, whose prognosis in an area without endodontic involvement is generally favorable.[1]

The granulation tissue was then removed with a very sharp curette, but penetration to the entire depth of this pocket was difficult.

A No. 8 round burr was then inserted to the bottom of the pocket, and at a slow speed all the remaining soft tissue was removed. Great care was taken to avoid cutting any tooth structure or the bony plate.

Fig. 5.

The osseous margin over the mesial root led to a sharp decline as it went distally (Fig. 3), reaching its most apical position at the mesial aspect of the distal root. To achieve a more physiologic contour, the alveolar crest of the mesial root was contoured to the level of the distal root, as were the interproximal areas. This allowed for deflection of food in these areas (Fig. 4).

After removal of all granulation tissue and recontouring of the bone, the osseous tissue was protected by Telfa[2] and covered with a thin layer of periodontal packing. The Telfa also served to protect the open bifurcated area from receiving any foreign bodies. Burlew dry foil was placed over the packing. Dressings were changed every week and removed after a three-week period (Fig. 5). No attempt to probe the area was made until eight weeks after the surgical procedure. At this time, a maximum depth of 2 mm. was recorded (Figs. 6 and 7).

Six weeks after the periodontal surgery, the patient returned for completion of the endodontic therapy. The six-week interlude was decided upon to allow ample time for healing. If healthy granulation tissue did form around the apices of the tooth, it would effectively wall off the apical foramina from any outside contaminants and permit complete sterilization of the canals.

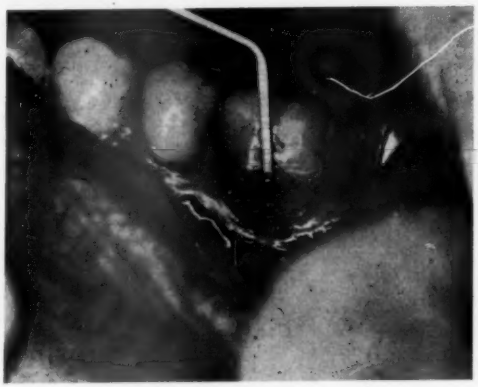

Fig. 6.

Fig. 7.

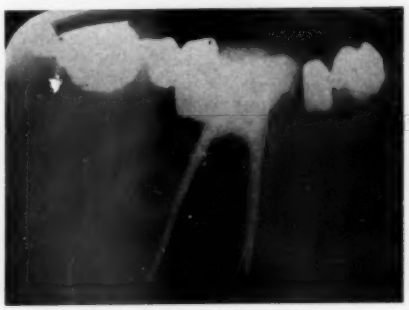

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Under sterile conditions, the canals were instrumented and medicated to remove any debris or coagulated blood that might have entered through the apical foramen during the periodontal surgery. On the subsequent visits cultures were taken and the canals were medicated. When two successive negative cultures were obtained, the canals were sealed with silver points cemented to position (Fig. 8).

Approximately one year following completion of the combined endodontic and periodontal therapy, the patient returned for re-evaluation of the tooth in question and replacement of the overhanging restoration. The clinical pictures at this time revealed the mobility pattern of this tooth to be less than 1 degree. There was a sulcus depth of 2 mm. on the buccal aspect (Fig. 9), and there was a well-adapted band of attached gingiva free of inflammatory changes at least 3 mm. in width. The area of the bifurcation involvement and infrabony pocket formation could not be probed.

Roentgenograms taken at this time showed an endodontically treated molar with complete filling-in of bone in the area of the bifurcation, reduction of the thickened periodontal membrane space, and elimination of the periapical area of rarefaction around the distal root (Fig. 10, taken before the filling was changed).

With the patient's consent, an exploratory procedure was performed to determine visually exactly how much healing had taken place. Two vertical incisions were made—one approximating the distal aspect of the mandibular left second premolar root and a second short incision approximating the mesial aspect of the mandibular left second molar. The flap was reflected with a periosteal elevator. The recountoured bony architecture achieved during treatment could be seen (Fig. 11). There appeared to have been complete filling-in of bone in the bifurcated area of the infrabony pocket (compare with Fig. 3). The flap was returned to its proper position and sutured. A periodontal pack was placed over the flap. Both sutures and pack were removed in seven days.

CONCLUSIONS

Recent advances in periodontal surgery and endodontics would suggest a re-evaluation of the prognosis of teeth so involved. In the past these teeth had a poor prognosis, but today many of them can be saved. A case so treated has been presented here. Close coordination between the endodontist and the periodontist, with a thorough understanding of the entire problem by all members of the team, must be established if these cases are to be treated successfully.

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PHYSIOLOGIC RESPONSE TO DENTAL STRESS

Irwin I. Ship, D.M.D., and Carl L. White, A.B.,** Bethesda, Md.*

REDUCTION of stress reactions in the dental patient has been the objective of numerous therapeutic measures proposed by clinicians, pharmaceutical interests, and equipment manufacturers. As a consequence, the need for a reliable method of appraising stress in the dental patient was emphasized by Ship[1] who, in a review of the literature and preliminary study, advocated further investigations in this field. The purpose of our study was to explore further the relationship between routine dental procedures and physiologic stress. This was measured as a function of adrenal cortical activity and was determined by measuring changes in the eosinophil levels in peripheral blood. The eosinophil responses of healthy adult subjects were observed during a variety of common dental procedures to study the relationship between various dental stresses and the magnitude of the eosinopenic responses and to elucidate further some of the factors involved. The modifications of these responses induced by barbiturate premedication and the administration of local anesthesia were investigated to define further the roles of pain, emotions, and tissue damage as components of dental stress.

Ever since Dalton and Selye,[2] in 1939, demonstrated consistent reductions in circulating eosinophilic leukocytes in the peripheral blood as a result of various alarming stimuli, the eosinophil response to stresses of various kinds has been broadly investigated. Surgical trauma, insulin hypoglycemia, hemolysis, hemorrhage, cold, epinephrine, labor, eclampsia, cesarean section, fever, electroshock, coronary occlusion, congestive heart failure, muscular activity, anoxia, and many other stresses have been shown to produce significant decreases in circulating eosinophils.[3-13, 15, 20] In human beings and in experimental animals, the magnitude of the eosinopenic response has been shown to vary directly with the degrees of stress.[3-7, 14, 15, 26] The lowest levels reached

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are seen three to six hours after the onset of a procedure.[3-8, 15, 26] Dreyfuss and Feldman,[16] Domanski and Nuttall,[17] Jouja, Stembera, and Cepelak,[18] and others[5, 6, 15, 19, 20-22] demonstrated that the emotions could play a large role in the eosinophil response to stress. On the other hand, physical exercise without emotional counterparts has been observed to cause eosinopenia.[12, 13, 15]

MATERIAL AND METHODS

The subjects, all healthy adults in need of dental treatment, agreed to submit to blood counts both before and four hours following their appointments. The eosinophil counts were performed using refinements of the technique described by Randolph[23, 24] which reduced the errors of counting.

All subjects were requested to perform their usual daily routines on the appointment days. Each subject rested in the clinic waiting room for several minutes before he was taken to an isolated clinic where all procedures were performed by one of us (I. I. S.) with the same dental engine, calibrated at 15,000 r.p.m. and operated with water spray. All appointments were made on a forty-minute basis and were varied as to time of day and day of the week. The patient had no foreknowledge of which dental procedure, if any, would be performed during an appointment.

Eosinophil counts were determined before and after every visit, including the appointment when the medical and dental histories were obtained, dental radiographs were taken, and an oral examination was performed. One appointment was devoted to oral prophylaxis which involved deep scaling. In selected cases, a second prophylaxis appointment was given, at which time polishing of the teeth was performed. All operative dentistry and oral surgery proceeded in sequence from tooth No. 1 (upper right third molar) to tooth No. 32 (lower right third molar). Regardless of the location of the tooth or the severity of the lesion, patients received one of the following prior to each operative procedure according to a randomized schema: (a) no injection, (b) injection of 2 c.c. 2 per cent lidocaine (no epinephrine), or (c) injection of 2 c.c. physiologic saline. The syringe was filled with the required solution without the dentist's knowledge of the contents. A code prescription based on the appointment number of each patient was arranged with the hospital pharmacy. Without the knowledge of dentist or subject, the pharmacy dispensed one of the following before each operative and surgical appointment: (a) no capsule, (b) a single, small red capsule containing 50 mg. pentobarbital sodium, or (c) a capsule of the same size, shape, and color containing lactose. The patient was told that the capsule would "calm his nerves" and was instructed to take it one-half hour prior to the next dental appointment.

All carious lesions indicated in the protocol for excavation and restoration were graded as to severity from 1 plus to 4 plus.

At various times during the sequence of operative and surgical appointments, visits were devoted to the polishing of restorations. Oral surgical procedures were limited to the extraction of teeth under local anesthesia (2 per cent lidocaine).

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At randomly selected intervals throughout this study patients were requested to remain at rest in the dental chair for the entire period of the appointment. The subject had no knowledge of when this would occur. The dentist was not present on these occasions, and the time was spent quietly reading or chatting with the dental assistant. However, the procedures for sampling of blood were the same.

RESULTS

Twenty-four subjects, sixteen men and eight women, attended a total of 255 dental appointments. With the exception of two patients with a history of penicillin sensitivity and another with a history of rheumatic fever in childhood, all subjects gave negative medical histories.

TABLE I. ANALYSIS OF PREOPERATIVE EOSINOPHIL COUNTS

PATIENT	SEX	AGE	N.	OBSERVED RANGE		MEAN EOSINOPHIL COUNT	S.E. OF MEAN
				HIGH	LOW		
D. D.	F	19	15	849.0	390.3	555.9	35.5
V. M.	M	35	11	706.7	98.0	383.2	59.6
F. K.	M	34	11	484.7	294.3	378.6	16.8
F. P.*	M	29	15	816.0	137.0	347.1	43.6
J. C.	M	25	14	492.3	151.7	343.2	28.2
H. A.	M	28	10	342.3	127.1	242.8	20.0
C. R.	M	32	8	283.3	86.7	193.7	22.3
G. H.	M	26	12	404.7	77.6	192.7	25.3
R. J.	F	28	5	316.3	35.3	184.0	33.9
S. W.	M	34	12	242.7	53.7	160.3	18.4
G. C.	M	32	15	277.7	81.3	146.4	13.9
M. M.	F	28	8	364.7	63.0	126.7	34.6
R. M.*	M	23	12	205.0	53.7	125.8	18.4
L. B.	F	31	14	179.3	60.7	116.5	10.8
J. W.	M	28	13	277.7	31.7	108.0	21.4
C. E.	M	42	17	166.5	18.0	87.5	9.7
H. W.**	M	29	13	153.2	29.7	75.7	9.0
A. B.	F	34	10	94.3	29.3	66.2	8.4
O. S.	F	30	7	74.0	24.3	59.3	6.4
E. C.	F	36	11	129.7	22.3	58.1	10.2
F. D.	F	34	7	76.0	39.0	54.7	5.1
A. C.	M	26	4	66.3	35.3	54.2	13.9
C. H.	M	28	3	63.0	35.0	44.4	9.3
R. W.	M	26	8	57.3	26.0	39.0	10.0
Mean		30.0	10.6			172.66	

*Past history of penicillin allergy.
**Past history of rheumatic fever.

The accepted normal range of eosinophil counts for healthy adults has been quoted as from 150 to 300 cells per cubic centimeter of blood.[25] Analysis of preoperative counts revealed far greater variations in the subjects under study (Table I), and individuals were found to differ significantly in total eosinophils. Time of day, day of the week, or season of the year did not affect the differences. The observed high or low preoperative counts were not correlated with the sequence of appointments or with any particular procedure. The number of eosinophils in the preoperative count had no influence on the

magnitude or direction of the postoperative response. Ingestion of pentobarbital sodium (50 mg.) one-half hour prior to blood count had no effect on the preoperative counts.

Analysis of eosinophil count responses to control appointments revealed a 28 per cent rise from morning to afternoon (Fig. 1). Eosinopenia was not observed following the interview appointment; nor was it seen after x-ray and oral examination. After initial prophylaxis, there was a mean decrease of 10.3 per cent, and a rise of 16.9 per cent was observed following the second prophylaxis appointment. This rise represented the only response to a dental procedure that was not significantly different from the control response.

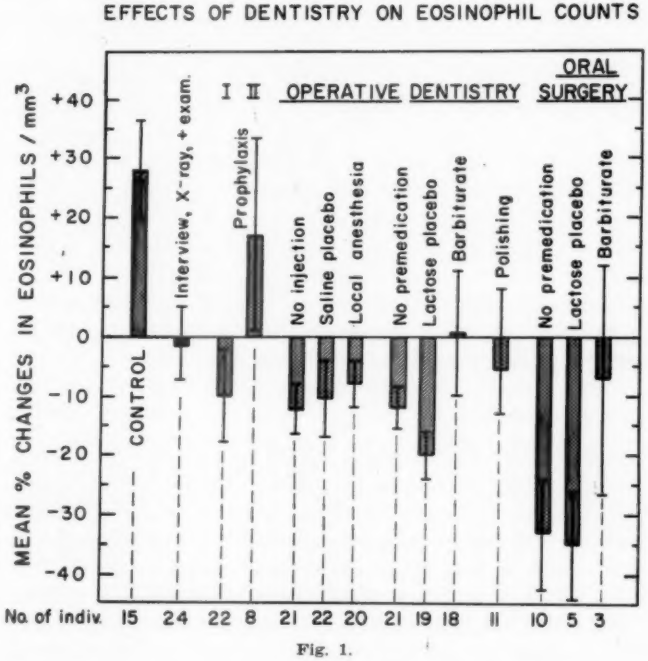

Fig. 1.

There were 124 operative appointments in which the effects of barbiturate premedication and local anesthesia were tested. Analysis of groups in which local anesthesia was administered revealed a mean decrease of 8.2 per cent. When no anesthesia was administered, the mean eosinopenia was 12.6 per cent. The group receiving saline placebo injections experienced a mean drop of 10.9 per cent. Analysis of the operative dentistry groups in which barbiturate premedication was given revealed a mean rise of 0.5 per cent. When no premedication was used, the mean eosinopenia was 12.0 per cent. The group receiving the lactose placebo experienced a mean drop of 10.1 per cent. The location of the tooth in the dental arch, the sequence of operative procedures,

and the severity of individual lesions had no effect on the magnitude of the eosinopenic response. All operative procedure responses demonstrated significant eosinopenia as compared with the response to control appointments.

The eosinophil responses related to the polishing of finished restorations revealed a mean decrease of 5.3 per cent. Although there were fewer subjects involved in the oral surgery groups, analysis of mean eosinophil count responses revealed significant changes. Two per cent lidocaine local anesthesia was administered prior to all oral surgical procedures.

When neither barbiturate nor placebo was taken, the mean eosinopenia was 32.9 per cent. The group that received lactose placebo experienced a mean decrease of 35.0 per cent. The patients who received 50 mg. of pentobarbital thirty minutes prior to the surgical appointment experienced a mean decrease of 7.2 per cent (Fig. 1).

One of the interesting and unexpected phenomena observed during the course of this study was the placebo effect. After opening of the blind studies, examination of patients' comments revealed that of forty-three cases in which placebo capsules were taken prior to operative and oral surgical procedures, reports of drowsiness or sleepiness were given in ten instances (23.2 per cent). Out of a total of thirty-six cases in which barbiturate capsules were taken in the same manner, drowsiness or sleepiness was reported on thirty-three occasions (91.7 per cent). A total of thirty-nine injections of saline were given prior to the operative procedures. Neither patient nor dentist was cognizant of the solution in the syringe during or after the injection. In six instances (15.3 per cent) adequate dental anesthesia was achieved.

DISCUSSION OF RESULTS

The physical and psychological factors accompanying a stress situation condition the individual response to that stress. Gofton, Graham, McGrath, and Cleghorn[26] divided the intensity of stress responses into three ranges. In the lowest there is no response, as the stress imposed is too slight to cause a response. Control observations in this study reflect this category. In the highest range the response is maximal, and no increase in stress can induce a greater eosinophil response. None of the dental stresses involved in this study fall into this range. In the middle range the patient's response varies directly with the severity of the stress. Dental stress falls within this range, and it is within this range that the various physical and psychological factors operate. It thus becomes important to evaluate three interdependent conditioning factors for their respective roles in the production of significant eosinopenia following dental manipulations: pain, tissue insult, and the emotions (anxiety, apprehension, and fear).

Pain.—In analyzing the pain-inducing potential of the various procedures, it was recognized that any subdivisions of dental operations were relative, depending upon the nature of the pain-inducing stress and the reactions of the individual patient. Nevertheless, it is obvious that neither the interview nor the manipulations involved in taking dental x-rays were painful. Examination

of the oral cavity was likewise a painless procedure. On the other hand, prophylaxis and operative procedures in the absence of local anesthesia could have been very painful. Although a 10 per cent difference is seen between the group responses to the interview, x-rays, and examination and to the first prophylaxis, this difference was not significant in view of the large amount of variation about the means. Since the size and severity of the various lesions did not play a role in the magnitude of the response in the operative dentistry groups, one might infer that pain, per se, was not a dominant factor in the eosinophil response. Although local anesthesia in the operative group modified the mean response by 2 to 4 per cent as compared with the means for the groups given saline and those given no anesthesia, this figure is of no statistical significance for the same reason.

The use of adequate local anesthesia in all oral surgical procedures should have discounted pain as a factor in the determination of eosinopenic responses. Nevertheless, the magnitude of the response was greatest in this group. This is essentially in agreement with the results reported by Ship.[1] However, barbiturate considerably modified the stress response to the levels seen in operative dentistry and prophylaxis. Certainly, further examination of the role of pain in dental stress is indicated.

It is interesting to note that in 15.3 per cent of total saline placebo dental injections profound anesthesia resulted, often exceeding four hours in duration.

Soft-Tissue Damage.—Soft-tissue damage has been indicated as having significant effects on the adrenocortical response to stress. Thorn and associates[15] and others[3-8] have reported on the profound effects of trauma and surgical operations on the levels of circulating eosinophils. In this study, soft-tissue trauma and damage were produced only in the oral surgery groups. The magnitude of eosinopenic response was effectively reduced when barbiturate premedication was administered. Soft-tissue trauma per se did not appear to be a significant factor in the stress responses to dentistry in this study.

Anxiety, Apprehension, and Fear.—Anxiety, apprehension, and fear have been found to play a significant role in causing eosinopenia. Dreyfuss and Feldman[16] demonstrated marked eosinopenia in senior medical students before entering final examination rooms. Jouja and colleagues[18] demonstrated significant eosinopenia in fifty-four women with chronic gynecologic complaints prior to operation. Domanski and Nuttall[17] reported significant eosinopenia in newly commissioned pilots after completion of F-86 fighter missions as compared with no response in experienced pilots after the same mission. The authors of these studies felt that the emotions would constitute a significant stress. In like fashion, the emotional response developing prior to, during, or after dental procedures must be carefully evaluated.

Since the subject had no knowledge of which procedure to expect before any visit, the emotional preparation for all dental visits was roughly equivalent. It is reasonable to suggest, however, that the psychological response to a painful procedure might alter the preparation for the next appointment. This did not appear to be a factor in this study. Demonstration of a significant difference

in the responses to all nonpainful dental procedures (interview, x-rays, and examination) as compared with responses to control visits indicates that fear and anxiety developing during the course of the dental appointment play a significant role. The modification of response induced by barbiturate in operative dentistry also indicates that emotions played a large role in stress responses, particularly since barbiturate had no effects on the preoperative counts. In oral surgery also, significant anxiety and fear must have developed during the course of the procedure, even though the duration of actual manipulation was considerably shorter than for any other group. The mean response to placebo was greater in both operative dentistry and oral surgery. On the other hand, barbiturate diminished the magnitude of the response. In oral surgery, premedication brought the level of response roughly to that experienced by the operative dentistry groups.

It is interesting to note the impressive number of instances in which placebo caused barbiturate-like subjective effects.

The absence of significant differences in the magnitude and direction of the eosinopenic responses resulting from the ordinary painful and nonpainful dental procedures studied (other than oral surgery without premedication) indicates that there are only small differences in these procedures as regards their stress-inducing components. The dental patient reacted similarly to all professional contacts with the dentist in his milieu. The significant differences demonstrated between responses to these procedures and to appointments in which the dentist was not personally involved (controls) indicate that he might be an important factor in this response and that neither barbiturate nor local anesthesia effectively modifies the response.

SUMMARY AND CONCLUSIONS

Physiologic stress in the dental patient was studied by comparing the changes in the eosinophil levels in the peripheral blood before and after various dental treatment and control situations. Eosinophil counts were performed prior to and four hours following interviews with patients, x-ray and oral examination visits, prophylaxis, operative dentistry, oral surgery, and control appointments during which no procedures were performed. The effects of local anesthesia and barbiturate premedication were compared with the effects of placebo and control appointments in operative dentistry and oral surgery situations.

Comparison of the stress responses among various treatment and control appointments revealed the following:

1. All dental procedures caused significant stress responses when compared with control appointments, with the exception of the second prophylaxis appointment.

2. Stress responses to various operative dentistry procedures were not significantly different from responses to interview, x-ray and oral examination, or prophylaxis appointments.

3. Local anesthesia had no effect on the stress reactions in operative dentistry.

4. Barbiturate premedication was associated with slight reduction in the stress reaction in operative dentistry, while placebo had no effect.

5. The stress reaction to oral surgical procedures was greater than the reaction to all other procedures tested. The effects of barbiturate premedication as compared with control and placebo groups were clearly seen in this group, reducing the stress response by 26 per cent.

6. Anxiety, fear, and apprehension during the course of the dental appointment appeared to be the primary factors involved in the stress-inducing aspects of dentistry in this study.

The authors wish to acknowledge the valuable assistance of Miss Virginia Moore and Miss Mary Alice Case in this project.

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ANNOUNCEMENTS

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First District Dental Society

The section on Oral Surgery will present a lecture by Herbert Bartelstone on "Pharmacologic Basis of the Management of Pain" on Wednesday, March 23, 1960, at 8 P.M. The lecture will be given on the eighteenth floor of the Hotel Statler in New York City.

Southwest Society of Periodontists

The fifth annual meeting will be held April 22 and 23, 1960, at the Western Hills Motel in Fort Worth, Texas. Drs. E. Cheraskin and Balint Orban will be the clinicians and will conduct an unrehearsed panel discussion. The subject is "Etiology and Therapy of Periodontal Disease."

For further information, please address John H. Swindle, Jr., D.D.S., P.O. Box, 3096, Westview Station, Waco, Texas.

Eleventh Mid-Atlantic States Conference on Dentistry

The theme of this year's conference, which will be held April 24 to 29, 1960, at the Hotel Hershey in Hershey, Pennsylvania, will be "The Contributions of the Basic Sciences to Current Clinical Practice." The following essayists will present the significant contributions of their particular fields:

Herbert K. Cooper, D.D.S., Sc.D., Professor of Cleft Palate Therapy, University of Pennsylvania; Director of Lancaster Cleft Palate Clinic, Inc., Lancaster, Pennsylvania.

Stanley C. Harris, Ph.D., Professor of Physiology and Pharmacology, Northwestern University Dental School; Professor of Physiology, Evanston Hospital, Evanston, Illinois.

Wilton M. Krogman, Ph.B., M.A., Ph.D., Professor of Physical Anthropology, School of Dentistry and Graduate School of Medicine, University of Pennsylvania.

John B. Macdonald, D.D.S., Ph.D., Director, Forsyth Dental Infirmary; Professor of Microbiology Harvard School of Dental Medicine.

Balint J. Orban, M.D., D.D.S., Professor of Periodontics, Loyola University School of Dentistry; Consultant, Fitzsimons Army Hospital and VA Hospital, Denver, Colorado; Histopathologist of Study Club, Chicago, Illinois.

George C. Paffenbarger, D.D.S., D.Sc. (Hon.), Praelector, Faculty of Medicine, St. Andrews University, Scotland.

Harry Sicher, M.D., D.Sc., Professor and Chairman of the Department of Anatomy and Oral Histology, Loyola University.

Enrollment will be limited. The fee is $300.00, which includes lodging, meals, and gratuities. Wives are invited; their fee will be $150.00.

Oral Pathology Laboratory of Mount Sinai Hospital

A clinical oral pathology conference will be held at 5 P.M. on Friday, March 11, 1960. The topic will be "Epithelial Tumor of the Jaws," and the speakers will be Drs. Lester Cahn and Leon Eisenbud. The conference will be held in Lecture Room 3-B on the third floor of the Administration Building, Mount Sinai Hospital, New York, New York.

University of Illinois

The College of Dentistry will offer a one-day course in crown and bridge prosthetics on Monday, June 20, 1960, under the direction of Dr. Stanley D. Tylman. Registration will be limited to ten. Tuition is $25.00.

Further information can be obtained from the Division of Postgraduate Education, University of Illinois College of Dentistry, 808 S. Wood St., Chicago 12, Illinois.

University of Oregon

The Dental School announces a program of graduate education leading to the Master of Science degree in the fields of anatomy, bacteriology, oral pathology, biochemistry, pedodontics, pharmacology, and physiology.

Within these department the program of instruction will be designed to provide additional experiences in basic courses, development of diagnostic skills, research to include thesis preparation, seminars and conferences, and supervised teaching. Arrangements with the University of Oregon Medical School permit the taking of specific courses, attendance at conferences, and use of the facilities of the Hospital and Outpatient Departments.

Only qualified persons who intend to make a career of dental teaching and research will be considered. Financial support, provided essentially by the National Institute of Dental Research of the United States Public Health Service, will vary from $4,000.00 to $5,500.00 per year.

Each applicant should send his *curriculum vitae* to the Program Director, Dr. Norman H. Rickles, Department of Oral Pathology, University of Oregon Dental School, 611 S. W. Campus Dr., Portland 1, Oregon.

University of Pennsylvania

The following postgraduate courses are announced:

Complete Denture Prosthesis. March 28 to 31, 1960. Vincent R. Trapozzano.
Endodontics. March 28 to April 8, 1960. Louis I. Grossman.
Applied Anatomy. April 20 to 22, 1960. Harry Sicher.
Minor Tooth Movement and Temporary Stabilization. April 20 to 22, 1960. Leonard Hirschfeld.
Complete Denture Prosthesis. April 25 to 29, 1960. M. M. DeVan.
Function—Prime Object of Dentistry. May 2 to 6, 1960. Arne G. Lauritzen.

Further information may be obtained by writing Dr. Lester W. Burket, Dean, University of Pennsylvania School of Dentistry, 4001 Spruce St., Philadelphia 4, Pennsylvania.

Traineeships Available at University of Pennsylvania

Research and teaching traineeships supported by the Public Health Service in the biologic sciences and in the comprehensive treatment and rehabilitation of the cleft palate patient are available at the School of Dentistry. Candidates for the traineeships in the biologic sciences must qualify for admission to the Graduate School of Arts and Sciences. These traineeships lead to M.S. or Ph.D. degrees.

The traineeship in the comprehensive treatment and rehabilitation of the cleft palate patients is clinically oriented; however, opportunities for course work in fields related to cleft palate therapy are available. If the trainee can qualify for graduate credit in the Graduate School of Arts and Sciences, course work may be applied toward requirements for M.S. or Ph.D. degrees.

Remuneration will vary, depending on the qualifications and needs of the successful candidates. Inquiries should be sent to the Chairman of the Committee on Traineeships and Fellowships, University of Pennsylvania School of Dentistry, 4001 Spruce St., Philadelphia 4, Pennsylvania.

Tufts University Announces Eleventh Berkshire Conference in Periodontology and Oral Pathology

The eleventh Berkshire Conference in Periodontology and Oral Pathology will be held June 19 to 23, 1960, at Eastover, a resort hotel in the Berkshire Mountains, at Lennox, Massachussets.

The two major topics for this year's Conference are "Medical Aspects of Periodontal Treatment" and "The Attainment of Physiologic Occlusion in the Total Treatment of Periodontal Disease."

The following clinicians will participate:

Charles E. Stuart, D.D.S., Ventura, California, who will devote two days to the subject of "Physiologic Occlusion."

Joseph L. Bernier, D.D.S., M.S., Chief, Branch of Dental and Oral Pathology, Armed Forces Institute of Pathology, Washington, D. C., who will present a clinicopathologic seminar dealing with "Oral Changes in Systemic Diseases."

Irving Glickman, D.M.D., Professor and Head of the Department of Oral Pathology and Periodontology, Tufts University School of Dental Medicine, Boston, Massachusetts, whose subject will be "Treatment of Periodontal Problems in Patients With Hormonal and Hematologic Disease."

Carl E. Cassidy, M.D., Assistant Physician, New England Center Hospital, Boston, Massachusetts, who will discuss "Patients With Endocrinologic Disease—Diagnosis and Medical Treatment and the Problems They Create for the Dentist."

William Dameshek, M.D., Director of Blood Research Laboratory, New England Center Hospital, Boston, Massachusetts, who will discuss "Patients With Hematologic Disease—Diagnosis and Medical Treatment and the Problems They Create for the Dentist."

Louis Weinstein, Ph.D., M.D., Chief, Infectious Disease Service, New England Center Hospital, Boston Floating Hospital, Boston, Massachusetts, whose subject will be "Patients With Infectious Diseases—Diagnosis and Medical Treatment and the Problems They Create for the Dentist."

For further information and application, write to Eleventh Annual Berkshire Conference, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Western Reserve University

The school of Dentistry announces the following postgraduate courses:

Crown annd Bridge Prosthesis. March 5 to 7, 1960. John F. Johnston. Fee, $100.00.

Oral Rehabilitation Using the P-M Instrument Technique. (Open to dentists and their technicians.) April 1 and 2, 1960. Arvin W. Mann. Fee, $100.00 plus $25.00 for technician.

Psychodynamics and Practice Administration in the Dental Office. April 23 to 25, 1960. Lloyd N. Hollander, William A. Lynam, Robert K. Stinaff, and Gerald H. Strate. Fee, $100.00.

Current Periodontal Therapy. June 2 to 4, 1960. Henry M. Goldman. Fee, $100.00

Closed-circuit television will be used in these courses where applicable. For further information and application, write to Director of Postgraduate Education, School of Dentistry, Western Reserve University, Cleveland 6, Ohio.

Albert Einstein Medical Center

The Department of Postgraduate Medical Education announces that a course entitled "Dentistry for the Handicapped Child" will be given by Morris Kelner, D.D.S., and associates on April 25 to 27, 1960. The course is designed to enable the dentist to render adequate and proper treatment for the handicapped child. Instruction will provide a fuller understanding of the pedodontic, pediatric, and psychologic factors as they affect the dental problem of the handicapped child.

The lectures will include a background of physical, mental, and emotional handicapping conditions; their oral manifestations; modifications in approach to chair treatment; modifications of techniques and methods of rendering adequate treatment; preparation of the patient and operator for total treatment under a general anesthetic in the operating room; periodontal, prosthetic, orthodontic, and speech problems; and psychosomatic and medicodental pediatric problems.

The course will be given at the Northern Division of the Albert Einstein Medical Center in Philadelphia, Pennsylvania. Registration, which is limited to ten students, will close April 10, 1960. The fee for the course will be $100.00.

Boston University School of Medicine

The Department of Stomatology, Division of Graduate Studies, School of Medicine, Boston University and the Massachusetts Memorial Hospitals, announces the following postgraduate courses:

Technics in the General Practice of Dentistry. Henry M. Goldman, David J. Baraban, Leo Talkov, Herbert Schilder, Gerald Kramer, Chester Landy, and Harold Berk. March 7 to 12, 1960. $175.00.

Advanced Course in Periodontology. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, and Jack Bloom. March 14 to 19, 1960. $250.00.

Full Denture Prosthesis. Chester Landy. March 28 to April 1, 1960. $150.00.

Periodontal Therapy. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Jack Bloom, and Associates. April 4 to 9, 1960. $175.00.

Apicoectomy—Surgical Endodontic Procedures. Herbert Schilder and Leonard Parris. April 18 to 22, 1960. $175.00.

Periodontal Pathology. Henry M. Goldman and Jack Bloom. April 25 to 30, 1960. $250.00.

Pulp Protection in Operative Dentistry. Harold Berk. May 12 to 14, 1960. $100.00.

Periodontal Prosthesis. Leo Talkov, David J. Baraban, Henry M. Goldman, Bernard S. Chaikin, and Gerald M. Kramer. May 16 to 20, 1960. $200.00.
Surgical Procedures in Periodontal Therapy. Lewis Fox and Associates. May 23 to 27, 1960. $200.00.

For further information, write to Director of Post-Graduate Studies, Department of Stomatology, Massachusetts Memorial Hospitals, 750 Harrison Ave., Boston 18, Massachusetts.

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REVIEWS OF THE LITERATURE

REVIEWS OF NEW BOOKS

American Men of Science. A biographical directory edited by Jaques Cattell. Tenth edition. Tempe, Ariz., Arizona State University.

The tenth edition of *American Men of Science* is in preparation. The A-E volume is now ready and other volumes will appear at intervals of no longer than nine months.

The directory will contain more than 120,000 biographies of American and Canadian scientists. Details will include name, address, field of endeavor, birthplace, degrees, positions held, society memberships, and research specialties. More than 40,000 of the biographies will be appearing in the directory for the first time, reflecting the startling growth of the sciences.

An advisory committee, sponsored by the National Academy of Sciences—National Research Council and the American Association for the Advancement of Science and under the chairmanship of Dr. Paul E. Klopskeg, is again helping to determine general policy.

K. H. T.

ABSTRACTS OF CURRENT LITERATURE

Correction of Fistula of Stensen's Duct. J. E. Erivin. Surg. Gynec. & Obst. 109: 247, August, 1959.

With the exception of paralysis of the facial nerve or one of its major branches, external salivary fistula is the most distressing nonlethal complication of surgical procedures in or near the parotid gland.

A simple procedure, first described by Fishler and Pogorel,* was used.

"The patient was taken to the operating room. The technique 'followed' was essentially that described by Fishler and Pogorel. The entire area around the fistula and the ulcer was infiltrated with 1 per cent procaine. The infiltration was carried through the entire thickness of the cheek. A U-shaped piece of No. 7 tonsil wire was inserted into the cheek so that the limbs of the wire straddled the external opening of the fistula. The two limbs were then passed completely through into the mouth so that they both appeared approximately 1½ centimeters from the old internal opening of the parotid duct. The ends of the wire were then twisted to prevent their slipping out. The patient experienced no pain during this part of the procedure."

The wire was removed intraorally one month later. The patient was followed for several months and found to have an excellent result.

T. J. C.

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*Fishler, H. W., and Pogorel, B. S.: Repair of Parotid Fistula, A. M. A. Arch. Otolaryng. 61: 331-332, 1955.

Adenoameloblastoma. Fumior Ono. Tr. Soc. Path., Japan **47**: 1015, 1959.

Adenoameloblastoma is a rare odontogenic tumor of which only three cases were reported by Masaki (two cases, 1939) and by Ito and associates (one case, 1957) in Japan.

The author reports the case of a tumor the size of a chicken egg, occurring in the anterior region of the left mandible in a 17-year-old girl.

Clinically, the tumor was suspected of being a follicular cyst. Microscopically, however, it was found to be a compact mass of many ill-defined nestlike aggregates of cells, each with a round or spindle-shaped nucleus. The cells in some of the aggregates were loosely arranged and stellate in form. The tumor tissue had lime salts deposited here and there in it, the cells collected in its different portions looking glandular in structure. The picture was indicative of an adenoameloblastoma.

The tumor in this case may have originated from the primitive oral epithelium made aberrant before its differentiation.

K. H. T.

A Clinicopathologic Study of Forty-three Cases of Glandular Tumors of the Tongue. P. M. Burbank, M. B. Dockerty, and K. D. Devine. Surg. Gynec. & Obst. **109**: 573, November, 1959.

Tumors of a glandular nature occurring on the tongue have, for many years, been lumped together in the category of mixed tumors. A series of forty-three glandular tumors, many of which had previously been diagnosed as mixed tumor, were classified into four groups on the basis of their histologic pattern. Cylindromas accounted for 51 per cent; mucoepidermoids, 26 per cent; and adenocarcinoma, 21 per cent. Only one mixed tumor was found in the series. All of the tumors with the exception of mixed tumors, must be considered as malignant, since they have proved to be capable of distant metastasis.

Excellent results followed radical surgical operations.

T. J. C.

Giant Cell Reparative Granuloma. H. P. Cook. Proc. Roy. Soc. Med. **52**: 43, September, 1959.

The author presents an interesting case in which an 11-year-old boy was found to have painless swelling of the mandibular left alveolus. X-ray examination revealed a lesion which involved the whole width of the mandible, extending from the alveolus to the lower border. The biopsy report indicated giant-cell reparative granuloma.

An operation was performed by an intraoral flap procedure. A cavity was present after removal of the tumor, and this was packed with bone chips made from "quick-freeze" homogenous stored bone. The flap was closed completely. A seven-day course of crystalline penicillin was given, 500,000 units intramuscularly twice a day.

An eight-month x-ray checkup revealed a well-consolidated bone, normal lip sensation, and no recurrence of disease.

T. J. C.

Management of Anterior Cranial and Upper Facial Injuries. G. S. Dugger and E. E. Peacock. Surg. Gynec. & Obst. **109**: 613, November, 1959.

Fractures of the zygoma are reported as being rare. "The zygoma is the heaviest bone in the face and when subjected to direct trauma, it usually dislocates from the zygomatic process of the temporal bone, the angular process of the frontal bone, and the maxilla. Following separation, the zygoma acts as a missile, moving through the center of the face, where it may smash the fragile bones in its path."

Partial trismus is suggestive of a depressed zygomatic arch.

Reduction of a fractured zygoma should be done, when possible, before the ninth day.

T. J. C.

The Biocenologic Approach to Black Hairy Tongue With New Concepts of Its Treatment. M. Lineback. Laryngoscope **69:** 1194, September, 1959.

"Black hairy tongue is not an isolated disease involving the tongue alone: it is actually a syndrome of the head and neck, with occasional manifestations in the genito-urinary, central nervous system, and with serious local extensions."

The treatment for black hairy tongue is the application of purified pancreatin in powder form, which is held on the tongue for periods of up to fifteen minutes. The average time required to restore the tongue to normal was ten days.

T. J. C.

Silver Implant In Situ Fifty-one Years After Resection of Mandible. M. Robinson. J. A. M. A. **128:** 890, October, 1959.

A case is reported in which a resection of the mandible was done fifty-one years ago and a metal prosthesis was inserted. The reason for the resection in 1908 was that "a giant-cell sarcoma had attacked the angle of the right half of the mandible." The patient was comfortable until 1950, at which time a mandibular molar tooth was removed under general anesthesia. The metal implant broke and the teeth would not occlude.

T. J. C.

Experiences With Vascular Abnormalities About the Parotid Gland and Upper Neck. Louis Rosenfeld. A. M. A. Arch. Surg. **79:** 533, October, 1959.

"Aneurysms and arteriovenous fistulae in the region of the parotid gland, pterygoid fossa and upper neck are rarely seen." Seven patients in whom such lesions occurred were seen over a four-year period.

In one of the cases reported, the patient had been in an automobile accident and had suffered a fracture of the left condyle of the mandible. At operation, the head of the condyle was found lying free within the sac and was removed. A diagnosis of false aneurysm of the external carotid artery was made. The second case involved a patient who had had an upper molar removed four years previously. There was profuse hemorrhage, which required hospitalization and transfusion. The findings were compatible with an arteriovenous communication.

Seven cases of vascular abnormalities involving the parotid region are presented. Two of the cases are of interest to the oral surgeon.

T. J. C.

The Oral Actinomycetes. K. A. Bisset and G. H. G. Davis. Arch. Oral Biol. **1:** 80, August, 1959.

"None of the infections of the teeth and associated tissues appears to be simple in its etiology. Not only do bacteria combine in complex physiological interrelationships but their pathogenic activity is greatly influenced by imponderable factors in the environment and constitutions of the host."

The name actinomyces was applied to the "ray fungi" causing the disease (actinomycosis) in man and cattle. The true actinomyces can be isolated from clinically healthy human mouths.

T. J. C.